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The Massachusetts Medical Society

The next Annual Meeting of the Massachusetts Medical Society will be held in Springfield, June 8, 9, 10, 1936.

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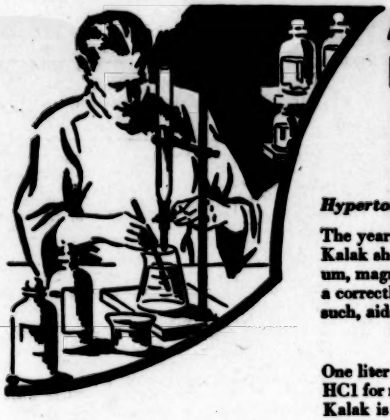

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**Bullowa, J. G. M. and Mayer, E.: J. A. M. A. July 20, 1935, Vol. 105, No. 3, p. 191.

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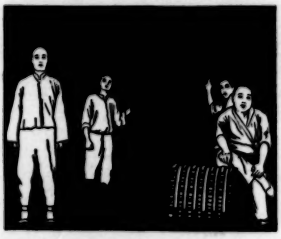

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The New England
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VOLUME 213 OCTOBER 24, 1935 NUMBER 17

PSYCHOPATHY AND THE GENERAL PRACTITIONER*

BY HORACE K. RICHARDSON, M.D.†

TO the practitioner of medicine, cases of mental illness and emotional disorder occurring among those who come to him for assistance constitute one of the gravest and most troublesome problems with which he is obliged to deal, because of their protean aspects and complex phenomena. These cases will naturally fall into two large nosological groups, namely, the psychotic, or those cases suffering with the frank mental diseases, and those that come under the general classification of the psychoneurotic.

About the first class, the psychotic, I shall have but little to say, because ordinarily they will present few difficulties in differential diagnosis, and the solution of them, from the viewpoint of the practitioner, is generally immediate commitment or hospitalization. Because of the gross interference with the usual mental habits, the very obvious changes in the common beliefs, personality expressions and mannerisms of the patient, the physician will rarely have much difficulty in convincing the members of his family that a serious condition is present. The coöperation of the family with the plan to hospitalize the patient usually will be easily obtained, and there should be little delay in its execution.

It is the latter group, made up of the various psychoneuroses, the baffling borderline cases and the innumerable emotional states and undefined, subtle maladaptations which disturb the lives and invade the homes of so many individuals, that will give the practitioner his greatest concern, tax his patience almost to the point of exasperation, challenge his resourcefulness to its maximum, and frequently require a high degree of sophistication and intuition for their solution. It is to this class that we shall devote our attention in this discussion.

Man's early mental life consisted almost entirely of efforts directed toward an understanding of the elemental forces of nature, and their effects upon his physical existence. As his intelligence increased, and he reached the stage in his development where he found it no longer necessary to devote the major part of his time to the pursuit of life-saving activities, he must have become aware of the fact that an inner being had been developing within himself, and for the first time he began to visualize an inner permanent, identifying quality, apart from his outside world. He began to experience the amazements of consciousness. We can very well imagine that in due course of time, he began to have ruminations relative to the various attributes of the conscious state, and to ponder and theorize upon its nature.

As the severity of life conditions softened, and man's interests broadened, he turned to the exploration of the neighboring country, and thus made contacts with other groups. This led to commerce. These activities brought riches, which in turn brought leisure; time in which the struggle for bare existence was temporarily suspended or anticipated, and in which opportunities for contemplation and introspection were presented.

We can imagine that the mystery of his personality occupied the mind of man to a greater and greater degree, and finally he began to discuss it with his fellows. Attempts at interpretation and explanation must have been largely colored by mysticism and the supernatural, but as experience broadened, his concepts became orientated and crystallized, and finally he developed the discipline of associative thought. The individual then began to be able to profit by his previous experience. Later the method of thinking called "Science" began to operate, and to be applied to various categories and conditions, of course without success of solution, because his problems were not yet susceptible of definite formulation. Centuries later, philosophy developed and finally became resolved into its fundamental elements, and out of these formulations the Art of Medicine originated.

As late as 470 B.C., when Sparta and Athens had joined forces and definitely turned back the advance of Oriental conquest and culture, and were able to give themselves up to the peaceful pursuit of philosophical speculation, their philosophy was confined almost exclusively to the physical aspects of life.

It was at about this point in the development of the world of ideas, that Hippocrates flourished, and it was at this time that he gave to Medicine its first indelible scientific impression. From out of the welter of medical superstition,

*Annual Alumni Address, Tufts College Medical School, May 10, 1935.

†Richardson, Horace K. — Assistant Medical Director, The Austen Riggs Foundation, Stockbridge, Mass. For record and address of author see "This Week's Issue," page 833.

theoretical assumptions, and the numerous philosophies concurrent with his time, he sifted out what he thought to be the factual material, and established the first synthesis of rational knowledge relative to the diseases and disorders of mankind.

Later, Socrates, 469-389 B.C., turned his investigative searchlight within, questioning, doubting, analyzing, not only the physical life of man, but especially his inner mental life, and as a result of his labors, gave to the world the compelling formulation, "Gnothe Seauton," "Know Thyself." This was a new and revolutionary attitude. It came to fruition during the Athenian period in the form of an encyclopedic interest in about every quality of man, including his psychic self and his dream life.

Plato anticipated Freud's interpretation of man's unconscious, the mechanism of repression, and of his dream life, as illustrated by the following quotation from his work: "Certain of the unnecessary pleasures and instincts are deemed to be unlawful; every man appears to have them, but in some persons they are subjected to the control of law and reason, and the better desires prevailing over them, they are either wholly suppressed, or reduced in number; while in other persons these desires are stronger and more abundant. I mean particularly those desires which are awake when the reasoning and taming and ruling power of the personality is asleep; the wild beast in our nature, gorged with meat and drink, starts up and walks about naked, and surfeits at his will; and there is no conceivable folly or crime, however shameless or unnatural—not excepting incest and parricide—of which such a nature may not be guilty. . . . But when a man's pulse is healthy and temperate, and he goes to sleep cool and rational . . . having indulged his appetites neither too much nor too little, but just enough to lay them to sleep . . . he is then least likely to be the sport of fanciful and lawless visions. . . . In all of us, even in good men, there is such a latent wild beast nature, which peers out in sleep."

After the fall of Athens, 404 B.C., there was a period during which Oriental fatalism and determinism flourished. During the period from 336-270 B.C., the philosophy of resignation of the Stoics, and the efforts of the Epicureans to nullify the painful in the psychic and physical lives of man, dominated the philosophic trends of thought.

Later came the Romans, the first of the pragmatists, and then the Christian ideal, founded wholly upon philosophical faith, in contradistinction to the wavering flame of scientific method, of searching for facts, that had just been ignited by the Greeks.

By the year 1096 A.D., the Crusades had begun, and the monastic attitude dominated the world of ideas. During the eleventh, twelfth and thirteenth centuries, the attitudes and interests of the majority of the peoples of the civilized world gradually, but completely, changed from those of the preceding centuries. With a fine ascetic disregard for the world, and the philosophies of materialism and the flesh, they were searching for solutions to the problems of the spirit, and in the salvation of their souls. The scientific method and the art of medicine went into a long period of scholastic lethargy.

The point I wish to make is, that for centuries, man had moved in and out of long periods of contemplation of either his physical self, his mental life or his spiritual awareness. Never had there been any broad propelling attempt to bring these three intrinsic fundamentals of man together, and to visualize him as a synthetic, biological entity. Each characteristic was isolated from the others in thought-proof compartments, and man, for the most part, looked upon each as having a separate existence and an independent function. There had been no concept of an integrated, interdependent relationship, or of a "total personality".

Spinoza, in the seventeenth century, made a definite attempt to destroy the distinction between an independent body and an independent mind and to eliminate this attitude of biological fragmentation. He attempted to create a "body-mind" relationship. The attitudes of the eighteenth and nineteenth centuries, slowly added impetus to the growing belief in the unity of man, but it was not until the early years of the twentieth century, when Sherrington published his monumental and revolutionary work, "The Integrative Action of the Nervous System," and Adolf Meyer established his epoch-making concept of psychobiological integration of the personality, that any real advance was made toward an understanding of the basic fundamentals of the personality or of the dynamics of mental disorders. Sherrington's efforts directed toward synthetic structuralization of nervous function, and the dynamic-genetic concepts of Meyer, together, materially clarified the situation, and for the first time in medical thought there was a definite discipline in our ideas of psychopathy and a rational basis for an understanding of their mechanics. The implications of integration gave a new philosophical insight into the origin and meaning of mental disorders. We had been looking at them too long from a pragmatic attitude alone.

For years man had thought of disease and disorder as occurring either within his mind or within his body. The interrelation between the mental and the physical had not been appreciated, and not until Sherrington and Meyer published their works, was there any real suggestion of psychosomatic correlation. We now recognize and appreciate the fact that it is this

integrative function of the nervous system that makes adaptation to life possible. Interferences with this integration make maladaptations to life equally possible, and it is through and by this integrated whole that they express themselves. It is likewise responsible for the mystery and the baffling incongruity of the symptomatology seen in many of the neuroses.

From the above, we conclude that there is in the central nervous system a centralization of the function of living, and of the life forces, due to a harmonious coördinated, regulated coöperation of all its parts. At this point a brief review of our knowledge of these parts may assist in a further understanding of the discussion of certain clinical aspects of psychopathy which is to follow.

For convenience, we separate the nervous system into three major divisions, namely, the brain, the spinal cord and the nerves. The latter are divided into the sensory neurons, the motor neurons, and the sympathetics. The function of the sensory neurons is to bring to the awareness of the individual, in the form of sensations, perceptions of his environment, as well as information relative to the state of his inner self. It is only through the sensory mechanism that man knows what is going on about him, or that he becomes aware of changes occurring within his own physical and psychic self.

The motor neurons, through the musculature, permit expression of man's will and desire in the form of conduct, behavior or action. They also serve various glandular structures. The sympathetics form the connecting link between the inner organic life of the individual and the higher, psychic functions of the central nervous system. They are closely related to the fundamental, archaic instinctive life of the personality, and represent an inheritance from the time when the early animal types had no thinking machine with which to adapt themselves to the circumstances of their environment.

The function of the spinal cord is similar to that of a great cable which provides specific pathways for the transmission of the sensory neurons coming in from the various end-organs, and going up to the brain, and for paths for the motor neurons coming down from the brain, and going out to the muscles, organs and glands. The sympathetics are also carried up and down within the cord, and within it, also, are various reflex arcs which make for certain automatic acts outside of consciousness.

The functions of the brain are as follows: first, the reception and transmission of nerve impulses, as in the reception of sensory messages, and the formation of perceptions, which are, in turn, transmitted to the motor centers as thinking, and to the hypothalamus as emotion or feeling, and secondly, the storing up of these messages in consciousness. No one of these three components is lost. Every sensation, every thought or idea, every emotion or feeling is stored up permanently in consciousness in the form of individual experience, and they are grouped together according to the law of association.

We are in the habit of speaking of various levels of nervous function, as for instance the psychological level, which is represented by thinking and the psychic life, and located in the cortex; and the vegetative, or physiological level, centered in the medulla, and represented by the more automatic functions of circulation, respiration and digestion. While these vegetative centres are located within the medulla, they are connected with the higher functions by neurons, and are being modified by psychic influences which flow to them in a constant stream from the cortical centres. In other words, between the higher and lower structural centres, and the various functional levels, associative neurons join all the numerous activities into a harmonious, well-coördinated, synthetic interrelationship, which functions for the good of the organism as a whole.

Now through all these structures, from the cortex down to the medulla, and through all the functional levels, from the psychological down to the physiological, there are two great antagonistic currents constantly playing; the one tending to initiate, maintain and express action; the other tending to stop, retard and repress action. Of their fundamental nature, we are in ignorance; they may be electrical. We know them only by their works. Without them, there would be no controlled life; with them, an efficient expression of the flow of energy within the nervous system is made possible. These two opposing influences are excitation and inhibition. In the vegetative system, we witness their effect in the excitant action of the sympathetics and the inhibitory action of the vagus on the heart rate. In the psychic sphere, we see the excitation of the instincts meeting the inhibitory forces of conscience.

It is the antagonistic character of these two principles that is responsible for the production of psychic conflict in man, and furnishes the basis for the origin and development of his maladaptations. An inharmonious relationship between the two lower levels of the personality, as represented by the habit patterns and the instinctive emotions, and the two higher levels, as represented by intelligence and conscience, always furnishes the causative background of the psychoneuroses. When this conflict is expressed through the effect of the emotions upon the sympathetic nervous system and the hypothalamus, the symptomatology becomes dominated by functional disorders, with the produc-

tion of unusual sensory disturbances in the organs, glands, joints, muscles, circulation, etc. When it is expressed through the cortical structures and functions, it takes the form of unusual psychic expressions as in obsessional thoughts and ruminations, phobias, compulsions, impulsions, fixed ideas and anxiety states. It is only to the former class that we shall devote our attention in this paper. We shall not discuss those cases which express themselves through the latter routes.

In view of all this, we must no longer think in terms of diseased organs within a man, but remember that we are treating a person as a whole in time-contact with the world about him. We are not treating an individual isolated from his environment or from his cultural, moral, economic and social past, but we are treating a person surrounded by many conditions and factors, and immersed in many influences, endogenous as well as exogenous, that tend to modify and determine the character of the total objective picture. We cannot separate an organically ill man from his habit patterns, his unconscious instinctive tendencies or his repressed conflicts, and therefore, when we attempt to treat a person with a diseased or disordered heart, for example, we must approach both the heart and the man together as a total situation, and in view of the effects that the above life factors have upon it. Again it is the integrative, dynamic, genetic aspects of the nervous system as a whole that make this attitude necessary and valuable. As Doctor Frederick Tilney has said: "In the main, we have made disease our chief interest. As a matter of fact, life is the principal theme, to which disease is but a corollary. The purely pragmatic attitude toward medicine is not without its defects. It fails to encourage an approach to the salient problems concerning the significance of life; it omits, as theoretical, the considerations of development and adaptation. Although it lends facility to professional administration, it does not establish the philosophical attitude upon which the advance as well as the practice of medicine ultimately depend."

It has been estimated that between fifty and seventy-five per cent of all cases of illness coming before the physician for assistance fall into the class of functional disorders of the nervous system. I have been informed by reliable persons that last year one of our large surgical clinics of the higher type turned back to referring physicians, for psychiatric investigation, fifty-six per cent of all cases sent there for abdominal operations. Investigation had failed to disclose the necessity for the surgical interference for which the cases had been originally referred. In our own work at the Riggs Foundation, each year we see a large number of cases which have gone through the gamut of surgical exploration, radical removal of organs, or internal investigations and treatment, with no subsequent amelioration of the sensory symptoms for which the procedures were instituted.

We receive many cases which have been diagnosed as organic, which prove to be, upon further study, hysterical conversions, or substitute reactions for repressed emotional states, and which are cured by the application of the proper psychotherapeutic methods. On the contrary, we also receive cases which have been diagnosed as hysterical, which prove to be organic. Many cases of postepidemic encephalitis fall into this class.

When we begin to investigate illness in the light of the above principles, we frequently discover startling correlations and amazing incongruities in human behavior, especially in those cases where adequate histories and skillful examinations are utilized as the basis for our interpretations. If I can leave but one valuable thought with you as the result of this hour, I hope it may be that you have been impressed with the necessity for making accurate and complete histories, and skillful and painstaking examinations, time consuming as they are. Carelessness in these two factors is responsible for many errors in diagnosis.

You are going to come in contact with many patients who come to you in your office, in clinic or in hospital, complaining of various pains, discomforts and disorders in different parts of their bodies, where complete examinations and accurate laboratory test, disclose no organic pathology whatever. Many times you will meet confusion, doubt and despair in attempting to arrive at a proper evaluation of the situation at hand. Frequently, it will take every particle of honesty you possess to treat these cases. Even after a consideration of all the facts at your disposal, often, diagnosis will be impossible. If you have learned to include in your routine examinations and histories, not only an account of the frank physical symptomatology, but in addition, facts relative to the life situations and environmental influences in which the person lives, something about his usual emotional reactions, his desires, hopes and ambitions; his discontents, his defeats and his inner habit patterns of reaction to responsibility, disappointment, frustration and failure, frequently, you will be surprised to discover causes for what otherwise would seem bizarre and inconsistent physical symptoms. You will bring about occasionally, what seem to be miraculous cures if you will but include in your histories, and give full value to the facts or psychic insult, as well as of physical trauma; to psychopathology as well as to physical pathology.

Just what should be our attitude and procedure, for example, in the following case that has lately come to my attention? Here is a man of forty years. He possesses an unusual degree of intelligence; he is well educated and has high cultural qualities. Apparently there is no reason why he should not be as happy as most of us. He has a nice family, a charming wife, an assured income, and has no special discontent with his social situation. Several months ago, he began to suffer with what he described as "spells", in which he suddenly finds his heart pounding, his breath coming in gasps, his pulse rate rapidly mounting to 120 per minute, and his body breaking out in drenching perspiration. At the same time he is consumed with what he expresses, as a "silly and unfounded paralyzing fear of impending disaster", and for days following the attacks, he is confined to his home completely incapacitated because of the actual physical discomforts associated with respiration and circulation, and because of a fear of a return of the so-called "spells". Repeated clinical examinations by reputable internists have failed to disclose any pathological conditions of any kind. Now what shall be our attitude? Shall we give him a prescription for a placebo of attractive appearance and fine flavor as a substitute for a cocktail before meals, or shall we tell him that there is nothing the matter with him, and that his attacks are "all imagination", and that he "must snap out of it", or "forget it"? Or shall we suggest that he take a long journey, or a sea trip, hoping that some kind genie will solve his problem for him before he returns? Or shall we take an intelligent, humane, scientific attitude toward this unhappy man and search for causes in fields other than in the purely organic? Not in the "body" alone, but in the "body-mind" machine; not simply in the physical realm, but in the psychic as well.

An investigation into the facts at our command in this case discloses some interesting data. We noted that his attacks began some months ago. In looking into the experiences of this man just prior to the onset of the attacks, we find that he had had no physical illness; in fact he reported that he had been feeling unusually well at the time. Nothing of any importance had happened to interfere with his domestic or social relationships. He had done nothing about which to be especially ashamed or sorry. There had been no reduction in income; on the contrary, he had just been promoted in the organization in which he worked. In his own mind, he had simply been taken suddenly ill with a physical disease, and no one had been able to discover its cause.

In going farther into the facts of his commercial life, however, we discover that his attacks first came on within one week after he had received this promotion. Could this have had anything to do with the onset? He thought not. "How could such a happy event", he said, "have anything to do with the production of the symptom picture" which we have described?

This man had served for several years as an efficient assistant to one of the department chiefs. He was well liked, accommodating, conscientious, coöperative and willing, and he possessed a wide fund of knowledge about the mechanics of the department in which he had worked. His chief was a domineering, efficient person, however, who made a practice of planning and directing most of the details himself. He was unable to delegate authority, or to take his assistant into his full confidence and therefore this able assistant had been trained in everything having to do with his work, except that of planning, exercising authority and assuming responsibility. When his chief died suddenly, and he found himself promoted because of seniority, to his position where he was obliged to assume all the responsibility for planning and directing, his personality suddenly demonstrated his inadequacy to carry this type of load. Unconscious emotional conflicts developed within himself because of the threat to his ego implied by the assumption of the responsibilities of his new position. Consciously, man cannot admit failure easily, and this man, therefore, repressed his fear of failure from his awareness. Unconscious processes then took up the problem and acted as though they had a will of their own, in that they seemed to have the power to get the individual out of the situation and at the same time save his personal pride. In this man, the emotional component of the complex, through its influences upon the sympathetics, set up a disturbance in the automatic functions on the physiological level, and produced the somatic symptom picture as above. As a result of what appeared to him to be entirely a physical illness, he was removed from the painful situation, and he left with no impairment of his self-respect and with no conscious realization of his inadequacy.

Now is this the whole story? No. It is not quite so simple as that. The promotion to the position of responsibility was simply the precipitating cause of the disorder. It simply reactivated and set in motion certain factors that were already in the personality make-up of the man at the time. The real source of his trouble lay deep within his personality structure in the form of habit patterns which were formed as a result of the environmental pressures, disciplines, admonitions and criticisms from those whom he loved or feared, before he reached the age of discrimination or judgment. Simply by the flight and pressure of time, they had been automatically pushed away into the unawareness, with the immature, non-logical emotional values formed in childhood still attached to them. Other pertinent facts included the influences of a father who had always criticized the

patient when a boy, a father who never encouraged his son, but who always derogated his ability, ridiculed his attempts at independence and unconsciously built into him habits of fear and retirement in response to situations of danger and responsibility. Just so long as the patient's chief assumed the responsibilities of the office, he was an excellent assistant, but when the time came for him to take up the load himself, his old habit patterns of fear, which had been lying in his unawareness, since childhood, suddenly assumed charge, and he developed an unconscious escape reaction in the form of circulatory and respiratory disorders. Escape is always the function of the neurosis.

Now there is another important factor in this and other situations of a similar character. Just how far is this man to be held responsible for his illness? Are we to look upon him as a weakling, as having no courage, as "yellow", as being morally responsible for his failure? Not at all. His entire conduct was motivated by forces entirely outside of his awareness and completely outside the influences of his own conscious will and logic. We must not hold these hypersensitive, neurotic individuals accountable for their disorders, until they have been given a true practical insight into the origin, nature and function of their symptomatology. Even after they have been given insight into these important factors, they must have developed for them, new habit patterns, new orientations and new purposive attitudes before we can hope to see them assume their rightful places in the competitions of life. The most difficult part of the entire situation is in giving these individuals the opportunity for developing this insight. This usually requires the assistance of a person accurately trained in the special method of psychiatric technique, known as free association. The function of the busy practitioner, in the severer cases of this nature, is generally that of diagnostician. And it is in this position that he can be of inestimable help and value to his patient, especially if he has developed the ability to evaluate these emotional situations early in their development, and thus be able to recommend treatment at a time when it assures the best possible prognosis.

Now I should like to cite another type of case with which you will be confronted frequently, and which will call for a high degree of courage and honesty to face. A young woman of thirty odd years appealed to her doctor for the relief of a constant feeling of muscular weakness and fatigue, and for vague, indefinite sensory symptoms in various parts of her body. She was a stenographer in the office of a busy executive. One morning, following a particularly difficult day, she awoke with the feeling that she had not rested well during the night. She got up slowly, however, and went to work. That afternoon she left the office early, went home and took a long nap before her evening meal. This sort of thing became more frequent, and the periods which she spent alone in her room, stretched out on the bed, increased. Finally she resigned from her position, spent most of her time in bed and sat up only occasionally.

For some weeks her family physician had been hunting for the source of her trouble. He had been unable to discover anything that could account for her continual sense of weakness except some suspicious teeth. These were removed and for a short period of time she felt improved, but not enough to be able to resume her work. Within a month she was back in bed.

About this time her family physician called in a fellow practitioner as consultant. In desperation they advised that the patient go to a general hospital for a complete physical survey. Here repeated examinations and tests disclosed nothing but a suspicious shadow in one of the frontal sinuses and a low basal metabolic rate. The sinuses were drained and the patient was put on thyroid extract tablets. Again she improved for a short period, but soon relapsed into her former state. Later a surgeon discovered a tender area over the appendix. A diagnosis of chronic appendicitis was made, and an appendectomy was performed. After a long convalescence, in which the sense of fatigue and the other sensations did not disappear, she returned to the hospital for the purpose of having adhesions broken up. This was repeated until there had been five abdominal operations within four years. The sense of fatigue never disappeared, the patient now was confined entirely to her room, and for the greater part of the time, had special diets and required constant attention. Fear of being alone had been added to her list of symptoms.

Finally her doctor recommended a "rest cure", and she was sent away to one of the usual "cures". Here she was placed temporarily in bed, given special diets, massaged twice daily, stuffed with food, washed out with high colonic irrigations every day, and at the end of two months, was returned home some twenty-five pounds heavier, stronger physically, and looking the picture of health, but still fatigued and subject to odd sensations in her body.

At last she was sent to a psychiatrist, boasting of the number of physicians she had seen, talking about the various operations she had undergone and mentioning the strange malady that no one had been able to cure. After considerable time spent in study of the case, the psychiatrist had discovered, among others, the following facts: for weeks, prior to the onset of her illness, she had been going through a difficult time with her fiancé, who vacillated between being nice to her and being impatient, angry and intolerant, and who had told her that he was not sure he desired to go on with the engagement into which they had secretly entered. Some time later, another stenographer, under whose supervision the patient had been

working, suddenly appeared in the office with an engagement ring upon her finger, and with the news that our patient's fiancé had given it to her.

It was on the day following the above reported episode that the onset of the fatigue syndrome appeared. The threat to this woman's ego was simply too great for her to tolerate. Her unconscious instinctive mechanisms got to work, interrupted the smooth running of the autonomic system and produced the sensory symptoms, the real origin of which had not been discovered. The ultimate purpose of the whole movement was to get the young woman out of the intolerable emotional situation of being a daily witness to the happiness of her former fiancé and her more successful rival. The associations attached to her work, her office and her former relationships became too painful to accept, consciously. It was then that the unconscious mechanisms began to operate, to remove her from the painful situation.

In an analysis of a thousand cases of so-called neurasthenia, it will be found that the outstanding symptom in at least eighty per cent of the cases, is an overwhelming sense of fatigue. Now this sense of fatigue is not real fatigue. Can we say that it is imagination? Not at all. What, then, justifies us in saying that it is not real fatigue? We all know that real fatigue is one of the most delicious sensations of the body. It produces a restful sense of relaxation, repose and peace. This sense of fatigue seen in the neuroses on the other hand, does not produce rest and relaxation; it brings on a continual restlessness, in which the person is tense and unable to rest, relax or sleep. In the former condition, rest results in a feeling of restoration of energy; in the latter, attempts at rest produce still greater sensations of fatigue and restlessness.

Neurasthenics are not suffering with real exhaustion, and they do not need rest or rest cures, as we ordinarily understand the term. Neither are they suffering with any organic changes within the nerve structures. In that state of mind known as the nervous breakdown, there is no actual structural breakdown in the nerves themselves. Rest only makes the individual even more sensitive to the sensory disturbances with which he is suffering. He needs change, perhaps, but he does not need rest. What he needs most is insight into the real, subjective dynamics of the symptoms, a better understanding of his personality and a better objective philosophy of life upon which to live.

This young woman for example, gradually recovered as she developed, over a period of several months, a real understanding of the subjective origin, nature and meaning of her symptoms, and when she began to live upon a well-planned, intelligent scheme of objective living. Frank recognition of the dynamics of her unconscious habit patterns and her personality defects, and an honest attempt to eradicate or modify them through a direct, voluntary attempt to keep her thoughts and acts relevant to a new objective, brought to her finally a degree of health wholly unimagined in her former mode of living. But see the terrific price she paid for her new knowledge. What an indictment that this woman was permitted to go through the painful diagnostic surveys, the needless surgical explorations and the economic loss of time, simply because no one took the time or trouble to inquire into the emotional circumstances of her life, and the habit patterns of her personality?

There is yet another interesting group of cases which falls into the class of sexual neuroses. The literature of modern medicine is filled with their descriptions. The following case taken from our own records illustrates certain of the polymorphic expressions of this type of difficulty.

A man of thirty-eight years, a graduate of one of the best eastern universities and of an excellent law school, comes for advice about a physical syndrome which invariably appears when he goes through a love affair. Three times in his life he had fallen in love and became engaged, and each time when the engagement was announced or plans were made for marriage he was obliged to withdraw from the situation because of the development of a prolonged "nervous breakdown" in which the outstanding symptoms were anxiety, with muscular weakness, dizziness, lack of concentration, nocturnal emissions, indecisions, terrifying dreams, headaches and anorexia.

After the third affair of this nature he began to suspect that the physical symptoms might have some correlation with the emotional condition concurrent with the episodes. Investigation into the facts of the case proved him to be correct in his assumptions. This man's father was a judge of a high court and also sat as an elector in the House of Bishops of a prominent denomination. He boasted about his "ideas" on the correct methods of bringing up children. For years his three sons were not permitted to leave the house after the evening meal. They were allowed but few opportunities to come in contact with the normal activities of boys and girls of their own ages except in those forms of entertainment occurring within the church society and under the strict supervision of correct chaperonage. They were made exceptionally dependent upon their mother in all things, and especially in their human relationships. The father frequently lectured to them about the "social sins" as he called them, and painted his descriptions of the sexual diseases in lurid colors. He told them with great seri-

ousness that the young man who had carnal knowledge of woman before wedlock was eternally damned in the eyes of the moral world. He explained that no one but a moral leper would dare kiss or touch the person of a woman except she be his wife. He built up such a pure, moral picture of woman and such a disgusting immoral picture of sex that not one of the three sons could bring himself to break through the unconscious forbiddenness which this ignorant man built up in their immature minds, and go into marriage. I am not complaining so much of the fact that this man told his boys something of sex as I am of how he did it. His motives were sound, but his technique was unforgivably stupid and its consequences almost permanent.

In his adult difficulties this patient was unable to break away from the non-logical habit patterns of thought that had been made for him by the hyper-moral and overemotional attitudes of his father, because they had been pushed so far away into his unawareness by the pressure of time that they performed, automatically, the non-conscious function of prohibiting him from making any prolonged or close relationships with a person of the opposite sex.

In each love affair the sexual stimulation brought about by the contacts with a woman released these old associations from the unwareness and influenced his conduct in such a way as to prohibit him from continuing the relationship. The censorship implied in the father-made attitudes which had not been brought to full practical maturation in the adult conscious world of reality produced in him prohibitions, inhibitions and incapacities in his later life. His anxiety represented the old, immature fear of parental disapproval and disfavor, and the physical symptoms reproduced the picture which he had retained from his father's description of "the wages of sin". The practical results consisted of the development of an inability upon the part of the patient to continue his relationships with women beyond the point of formal social contacts.

We see also many cases in which the unresolved ideas relative to the auto-erotic practices of childhood and adolescence prevent both men and women from entering the marriage state because of the neurotic fear that they have injured their sexual organs. Many of these misinformed individuals feel that they would be unable to carry on a normal sex life implied in marriage, and become impotent or frigid, and never marry.

Finally, there is another group of cases the importance of which is rapidly growing in the minds of the medical profession. Ordinarily when we think of diseased processes we think in terms of disordered structure and function. We have difficulty in thinking of one without the association of the other, and when situations arise in which both are involved, we have been in the habit of expecting the disorder in structure to precede the disorder in function. In the class which we are now considering it is known that the change in function precedes the change in morphology, and that long-continued excitation of the structures by anomalies in function ultimately produces serious pathological changes in structure. Moschcowitz, in the *New England Journal of Medicine* for April 4, 1935, lists these conditions as follows: (1) Essential hypertension; (2) "Graves' syndrome"; (3) Gastric and duodenal ulcer; (4) Cardio-spasm; (5) Spastic or irritable colon and mucous colitis. Probably from the purely pathological aspect these five types are more or less related through changes in the blood and muscle supply caused by long-continued vasomotor malfunction.

Long ago Dr. Walter B. Cannon in his book, "Bodily Changes in Pain, Hunger, Fear and Rage", showed us the consistent visceral changes that accompany emotional reactions, and proved that affective states have a very definite effect upon the chemical balance of the blood and the endocrine glands. Pavlov's experiments with the conditioned reflexes have demonstrated beyond doubt that situations outside of the body touching upon the archaic autonomic mechanisms have definite influences upon the operation of the secretions and glandular structures. The work of Dr. Walter C. Alvarez at the Mayo Clinic gives ample evidence that life situations of certain types have definite effects upon the physiological functions. The work of Draper and McGraw has demonstrated that there may be psychic patterns of personality synchronic with the development of gall bladder disease and gastric ulcer. Maurice Fremont-Smith, Lawrence K. Lunt, Austen Riggs, Woodyatt, Nellis B. Foster, C. C. Wholey, Lauren Smith and many other writers of authority have given us undisputed evidence of their experiences in reporting cases wherein emotional conflicts, unresolved immature habit-patterns and blocked instinctive strivings have expressed themselves as obstruction of the bowel, sexual impotence, heart dysfunction, digestive interferences, muscular weakness, circulatory troubles, pain habits, high blood pressure, etc. The following case illustrates certain of these relationships.

Mr. I., aged fifty. Ten years ago suffered with what was diagnosed as gastric ulcer. Recovery was complete and the patient was free from symptoms for ten years. In 1929, at the time of the industrial and financial emergency, his South American export business failed and his holdings of stocks and bonds became depleted. He was obliged to discharge his large corps of servants, sell his palatial home, and move into a modest apartment, where his wife was obliged to do all the work. She did not take kindly to this great change in her life. She was suddenly

reduced from a position of great ease and luxury to one of hard labor, from a position of social prominence to one of almost total obscurity, and her adaptive abilities failed her. As time went on she lost her equanimity and became irritable and intolerant. She nagged her husband to the point of exasperation, blamed him for the loss of his business and called him a fool and a knave. As time went on she became so unpleasant he spent most of his time away from home, and then she accused him of infidelity. After several months of this sort of thing he began to lose his appetite and sleep, and became unable to concentrate upon any matter of business. One day while at dinner, after a particularly disturbing scene with his wife, he developed a sudden and sharp pain in the epigastrium, vomited his meal and went into a state of collapse. That night he had a large copious stool of clear mucus. The local physician made a diagnosis of gastric ulcer and acute colitis, and at once began to treat the patient for this condition. After several weeks of illness and without any appreciable improvement the man was sent to a hospital. Here no evidence of ulcer could be discovered in spite of the fact that all the subjective symptomatology continued. Finally he was turned over to a psychiatric group for study and recommendation. For days the gastric pain and mucous colitis continued. The patient was unable to retain much food and the mucous stools finally became filled with blood. Still no evidence of organic pathology could be discovered. Psychotherapy was continued and finally the man began to improve. As the causes for the emotional situation were gradually removed and as the patient gradually developed insight into the real nature of his troubles he slowly began to recover. After many weeks of continued treatment he left the hospital weighing some forty pounds more than upon admission and in an excellent condition of mental and physical health.

Cases of this type are exceedingly common. We believe that at least ninety per cent of all cases of mucous colitis are of psychogenic origin. Cannon was able to produce intestinal stasis in cats at will simply by throwing them into violent states of fear or anger. Many of us know the distressing feeling of precordial pain in situations calling forth the deep emotions of grief. The rise in blood pressure and the quickened pulse in fear are matters of universal experience. The empty, "all gone" feeling in the pit of the stomach during violent anger is too common to need discussion. The sudden vertigo, with unconsciousness, in the hypersensitive person is an experience in the lives of many people. During the World War men frequently got up in the morning to find their thyroid glands enlarged to alarming proportions because of the fear aroused by the news of an impending advance or attack. We all know of the hysterical paralyses, the emotional conversions and the changes in the dermal circulation due to affective states. Those of you who read the unexpurgated edition of "All Quiet on The Western Front" will remember the example of uncontrolled bowel movement in the new recruits.

Now all these conditions demonstrate the fact that it is the emotional conditions and situations that precede changes in function, and it is the long-continued, persistent changes in function that may, and often do, lead to changes in structure. In writing of certain difficulties in the knee joint Dr. Austen Fox Riggs says, "Furthermore, from the beginning the function is still further curtailed by the fear that anything but the gentlest use of the joint may cause damage. If this condition persists for any length of time, a secondary physical change takes place in the joint itself."

So, in your work as medical men, do not get into the demoralizing habit of depending entirely upon what your instruments of precision and the laboratory reports tell you. Remember that you are dealing with a total personality, all of whose factors cannot be measured with mathematical absolutism. One must develop the habit of feeling into the emotional and psychic factors as well as into the physiological facts. Treat the total man, not the disease. Learn to look upon man as more than simply a physical machine.

You will have many psychological points of view and various philosophical postulates upon which to make your interpretations, but do not put exclusive dependence upon any one school. Remember we have some ten or fifteen primary instinctive tendencies and any one of them may be at the bottom of the maladaptive conflicts. Bear in mind that there is one school of psychological thought that has no textbook and no exclusive leader. It is the school of meticulous care and common sense.

DIATHERMY IN LOBAR PNEUMONIA*

Preliminary Report

BY WINTHROP WETHERBEE, JR., M.D.,† JOHN A. FOLEY, M.D.,† AND JOSEPH RESNIK, M.D.†

INTRODUCTION

DURING the past decade or thereabouts there have been numerous reports in the literature dealing with the use of diathermy in the treatment of lobar pneumonia. The various observers have shown considerable difference of opinion as to the value of this measure, but are almost unanimous in their belief that it is valuable symptomatically, and that it is not harmful when properly used.

Stewart[1], perhaps the staunchest advocate of this method of treatment, has reported a series of over a thousand cases, with a mortality of 11.9 per cent as opposed to the 28 per cent mortality commonly observed in hospital cases of pneumonia treated by other methods. Harbin[2] mentions a series of sixty cases, with a 12 per cent mortality. Lilien[3] believes that diathermy is sufficiently valuable to be indicated in all cases, except aspiration pneumonias, or lobar pneumonias with complicating pulmonary abscess, closed empyema, or cardiac decompensation.

Other workers have been only slightly less enthusiastic. Robinson[4], while he does not find the duration of the illness shortened to any extent, observes relief of pain, increased tendency to rest and sleep, less need for sedatives, and a general improvement sufficient to justify its use. Simon[5] finds no specific response to diathermy, but sufficient general increase in the comfort of the patient to make it a valuable symptomatic measure. All agree that under the direction of a competent physician it is an absolutely safe procedure.

Because of these favorable reports, it was decided to use diathermy in the treatment of lobar pneumonia on the Fifth Medical Service of the Boston City Hospital during the winter of 1934-35.

SELECTION OF PATIENTS

All of the patients with lobar pneumonia were given the standard treatment, including serum and/or oxygen when indicated. (With the exception of one case, the latter was given by means of the oxygen tent rather than by nasal catheter.) In addition, one half of the series were given diathermy. The candidates for diathermy were not selected, but were alternate cases.‡ The stage of the disease, the extent of lung involvement, the type of organism, and the general condition of the patient were not considered, and an attempt was made to render the selection as nearly as possible one of strictly controlled cases. One or two patients who were moribund on admission and died within a few hours, were omitted from each of the groups in this report.

As soon as a patient was admitted and the diagnosis of lobar pneumonia made, the Department of Physiotherapy was notified, and if the patient was a candidate for diathermy it was started promptly, in some cases within a few minutes, and in every case within a few hours.

No patient was included in either group of this series, in whom the clinical diagnosis of lobar pneumonia was not corroborated by x-ray.§

TECHNIQUE AND EFFECTS OF TREATMENT

Diathermy is a method of generating heat in deep-seated tissues by passing through them high frequency currents. The heat employed is not obtained, as such, from a source outside the body of the patient but is generated in the tissues proper, as a result of the electro-magnetic energy which oscillates through them at a very high rate of frequency[13].

Of late, the terms short-wave diathermy and ultra-short-wave diathermy have come into prominence. The former refers to wave-lengths of approximately 30 to 12 meters while the latter comprises of the range, 12 to 2½ meters. In terms of frequency the present-day apparatus produces currents of ten million to one hundred million oscillations per second[14].

For these currents Drs. Schliephake and Reiter have claimed selectivity and specificity. By selectivity is meant that high frequency currents of given wave-lengths will cause optimum heating effects of corresponding body tissues; while specificity implies that these currents produce, in addition to heat production, specific biologic effects on the tissues analogous to inflammation, combating sepsis[15, 16].

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‡There were a few exceptions to this, as for instance when a patient was admitted just before a week-end or a holiday, and it would not have been possible to start the diathermy as promptly as in the other cases. These patients were then used as controls, and the next two or three in succession were included in the diathermy series, until the two groups were even again. For all practical purposes, however, we may regard the selection as one of alternate cases.

§A single exception to this was the patient "E. L.", in the control group, who had her crisis on the second day in the hospital; the chest plate was not taken until three days after this time, and was read as negative. We felt that the history and physical signs in this case were sufficient to establish the diagnosis, and that an x-ray taken earlier would have confirmed it.

In our series we employed orthodox diathermy obtained from high-frequency of one million oscillations per second; giving a wave-length of approximately three hundred meters. Under these circumstances whatever changes occurred in the conditions of the pneumonia patients, in all probability were brought about by the generation of heat resulting from the application of diathermy and not from selectivity or specificity.

That heat causes dilatation of blood vessels with resulting local hyperemia can be readily observed on the surface of the body when any form of heat is applied to it. It is, therefore, not unreasonable to expect similar changes in deep-seated tissues which are heated by diathermy, namely, the consolidated portions of the lungs in pneumonia. By the same token expansion of the air-spaces in the lungs occurs with resulting augmented oxygenation.

A portable high-frequency machine was carried on a truck to the wards where treatment was administered. This truck was equipped with a rotary converter of one kilowatt to change the ward D. C. to A. C. The electrodes used were comprised of pliable block tin, about 20 gauge. They were covered with soap lather and applied anteroposteriorly with the smaller electrode nearest to the consolidated area. The dosage was sixty to one hundred milliamperes per square inch of contact area of the smaller electrode[17, 18]. Thus in the average case one thousand to fifteen hundred milliamperes were used. The duration of the treatment was one-half hour and was repeated twice, daily. The average number of treatments per patient was eight; giving a total of four hours of diathermy. It is apparent that from the standpoint of time the sacrifice made is not exorbitant compared with the beneficial results derived from this measure.

In this discussion we are concerned neither with laboratory findings nor the underlying theories, as much as we are interested in the actual clinical findings. The latter were gratifying.

In all but two cases of the diathermy group the treatment induced marked perspiration. Obviously this is a form of elimination, relieving the load of other organs concerned in this process. The patients while under treatment volunteered the information that the tension or pressure in the chest was lessened during the seance. The breathing was less labored and deeper, probably due to the relaxation and relief from pain brought about by the heat.

In general, comfort to a certain degree seems to have been secured.

When presence of fluid in the chest was detected pointing to empyema we did not deem it advisable to continue with diathermy[3]. Instead, ultraviolet radiation was resorted to as a method of building up the resistance of the body to the infection[19, 20]. The latter was given with a quartz-mercury lamp in four exposures, namely, from waist-line up and waist-line down anteriorly and posteriorly.

Although we discontinued the use of ordinary diathermy when empyema was encountered we are inclined to believe that it is worth trying the shorter wave-length diathermy for which, as explained, selectivity is claimed. Dr. Schliephake[15] reported that similar conditions, in his experience, responded favorably to short-wave therapy.

ANALYSIS OF RESULTS

	Diathermy Group	Control Group
Occurrence of empyema	Three cases (16.6 per cent)	Four cases (22.2 per cent)
Number of patients who received serum	Seven (38.8 per cent)	Four (22.2 per cent)
Number of patients who received oxygen	Five (27.7 per cent)	Eight (44.4 per cent)
Number of patients who received both serum and oxygen	Four (22.2 per cent)	Three (16.6 per cent)
Termination by crisis	Eight (44.4 per cent)	Seven (38.8 per cent)
Termination by lysis*	Six (33.3 per cent)	One (5.5 per cent)
Average duration of fever in uncomplicated cases†	5.7 days	6.0 days
Number of deaths	Two	Six
Mortality	11.1 per cent	33.3 per cent

*Although the effects of diathermy in our series agreed in the main with those noted by other observers, a striking exception occurred, in that while Stewart[1] found that the fever terminated by lysis in 97 per cent of his patients, our percentage was very much lower (33.3).

†This does not include fever prior to admission, but its duration in the hospital.

Further data is supplied in tables 1 and 2.

COMMENT

In a paper published thirty-four years ago, Sears and Larrabee[9] of this hospital reported the mortality of a series of over nine hundred consecutive cases of lobar pneumonia as 35.9 per cent. Excluding those patients who were moribund on admission, the mortality was 29.1 per cent.

In 1934, Stewart[1] stated that the mortality from lobar pneumonia in hospital practice is 28 per cent. With this approximate figure there is general agreement at the present time[7, 8, 9, 10].

TABLE 1

CONTROL GROUP

	Patient and Hospital Number	Age	Sex	Color	Date of Onset	Date of Adm.	Cond. on Adm.	Lobes Involved	Sputum Type	Blood Culture	Oxygen	Serum	Complications	Duration of Fever	Termination	Remarks	
1.	T. G. 768226	20	M	White	10-3	10-4	Poor	RM	I	Pos.	———	#	None	10 days	Recovery (Lysis)	Patient extremely ill on admission; toxemia much greater than amount of lung involvement would indicate. Discharged on 23rd day.	1.
2.	G. B. 769934	35	M	White	12-9	12-12	Poor	RU, RM, RL	II	Pos.	#	#	Empyema Toxic neuritis	30 days	Death	Patient a chronic alcoholic. Three previous attacks of pneumonia.	2.
3.	J. J. S. 771424	52	M	White	12-26	12-27	Poor	RL, RM	III	Neg.	———	———	Uremia	6 days	Death	Patient had leucopenia, elevated NPN on admission. Developed anuria and was pronounced on sixth day.	3.
4.	J. J. 771566	27	F	White	12-23	12-29	Fair	RL	XII	Neg.	———	———	None	3 days	Recovery (Crisis)	Discharged well on 14th day.	4.
5.	F. D. 771774	50	M	White	12-30	12-31	Poor	RL	III	Neg.	#	———	None	9 days	Recovery	Convalescence prolonged, and patient not discharged until five weeks after admission.	5.
6.	E. M. 772909	34	F	Col.	1-7	1-11	Fair	RL, RM, LL	XX	Neg.	———	———	None	8 days	Recovery (Crisis)	Positive Kahn test. Discharged 2-2-35.	6.
7.	C. B. 773394	53	F	Col.	1-12	1-15	Fair	RL, LL	XII	Neg.	———	———	None	6 days	Recovery (Crisis)	Discharged well 2-6-35.	7.
8.	F. C. 774150	50	M	White	1-18	1-22	Poor	RU, RM, RL	II	Neg.	#	#	Toxic psychosis	12 days	Recovery	Patient ran a septic type of fever, falling gradually to normal over 12 days. Discharged well 3-7-35.	8.
9.	R. B. 774699	52	F	White	1-25	1-28	Good	RM, RL	VIII	Neg.	———	———	None	7 days	Recovery (Crisis)	Convalescence uneventful. Discharged well 2-16-35.	9.
10.	H. E. 775585	40	M	White	2-1	2-5	Fair	RU, RM, RL	I	Pos.	#	#	Atelectasis	4 days	Death	Patient ran a stormy course, was toxic and cyanotic throughout, and was pronounced on fourth day in hospital.	10.
11.	C. M. 775597	39	F	White	2-2	2-5	Poor	RM, RL	a.	Neg.	———	———	Pyelonephritis Uremia	—	Death (Crisis)	Patient had crisis on seventh day; well for a week, then developed pyelonephritis, and uremia. (Was five months pregnant.) Pronounced 3-24.	11.
12.	B. McD. 776046	32	F	White	2-5	2-9	Poor	RL, LL	XXII c.	Neg.	#	———	None	4 days	Death	Patient did not respond to treatment, and was pronounced on fourth day.	12.
13.	L. Q. 776066	53	M	White	2-5	2-9	Poor	LU, RL, LL	XIII d.	Neg.	———	———	Empyema	—	Recovery	Patient developed empyema, was transferred to surgical service for rib resection, from which he recovered satisfactorily.	13.
14.	J. H. 776346	45	F	White	2-11	2-12	Poor	RU, RM	VII	Neg.	#	———	Delirium tremens	2 days	Death	Patient a chronic alcoholic, developed D.T.'s on second day. Kahn was positive. NPN 80.	14.
15.	M. C. 777624	23	F	White	2-23	2-24	Poor	RL, RM	XXII	Neg.	#	———	Empyema	—	Recovery	Patient ran a septic type of fever for weeks. Empyema finally cleared after being aspirated several times. Discharged 4-24.	15.
16.	E. L. 783188	17	F	White	4-15	4-18	Good	RU, RM	b.	Neg.	———	———	None	3 days	Recovery (Crisis)	Discharged well 4-25.	16.
17.	M. McC. 778769	46	F	White	3-3	3-7	Poor	RL, RM	b.	Neg.	#	———	Empyema	—	Recovery	Patient had closed thoracotomy, recovered.	17.
18.	J. O'B. 782817	39	M	White	4-9	4-15	Good	RL, LL	b.	Neg.	———	———	None	2 days	Recovery (Crisis)	Discharged well 5-6.	18.

a. Hemolytic streptococcus.
b. Sputum not obtained.
c. Sputum also showed b. influenza.
d. Sputum also showed b. influenza and streptococcus viridans.

TABLE 2

DIATHERMY GROUP

	Patient and Hospital Number	Age	Sex	Color	Date of Onset	Date of Adm.	Cond. on Adm.	Lobes Involved	Sputum Type	Blood Culture	Oxygen	Serum	Complications	Duration of Fever	Termination	Remarks	
1.	J. G. 770408	49	M	White	12-14	12-17	Poor	LL, RL, RU, RM	VIII	Pos.	±	— —	Empyema	—	Recovery	Patient had bronchiectasis.	1.
2.	J. H. 772219	21	M	White	1-3	1-4	Poor	RU, RM, RL	I	Pos.	±	±	None	8 days	Death	Patient desperately ill on admission, and did not respond to treatment.	2.
3.	R. W. 772253	19	M	Col.	1-3	1-4	Fair	RL, LL	a.	Neg.	— —	— —	None	6 days	Recovery (Lysis)	Discharged well 1-21.	3.
4.	R. F. 772724	21	F	White	1-7	1-9	Fair	LU, LL	I	Pos.	±	±	Empyema	—	Recovery (Lysis)	Prolonged convalescence. Discharged 3-18.	4.
5.	M. F. 773155	23	F	White	1-6	1-13	Good	RU, RM RL	I	Neg.	±	±	None	14 days	Recovery (Lysis)	Discharged well 2-24.	5.
6.	N. W. 773189	16	F	White	1-9	1-13	Poor	RM, RL, LL	a.	Neg.	— — —	— —	None	19 days	Recovery (Lysis)	Patient had a marked secondary anemia. Discharged well 3-3.	6.
7.	L. M 773898	27	M	White	1-15	1-20	Fair	LL, RL	XVII	Neg.	— —	— —	None	3 days	Recovery (Crisis)	Crisis on third day in hospital. Normal convalescence. Discharged 2-6.	7.
8.	A. A. 777131	61	F	White	?	2-19	Poor	RL, RM	b.	Neg.	— —	— —	None	3 days	Recovery (Crisis)	Patient had had a "cold" for three weeks prior to admission, and date of onset of pneumonia could not be determined.	8
9.	M. L. 778858	17	M	White	3-4	3-8	Fair	RL	VII	Neg.	— —	±	None	4 days	Recovery (Lysis)	Discharged 3-22.	9.
10.	L. S. 779437	20	M	White	3-8	3-13	Poor	LL, RM, RL	XIV II	Neg.	— —	±	Empyema—Iritis Serum reaction	—	Recovery	Patient developed arthralgia and urticaria after receiving serum. Discharged well 4-6.	10.
11.	R. S. 782331	43	M	White	4-7	4-10	Poor	RL, LL	I	Pos.	±	±	None	3 days	Death	Leucopenia. Patient very ill on admission, and did not rally. Pronounced on third day in hospital.	11.
12.	J. F. 782052	50	M	White	4-5	4-8	Fair	RM, RL	III	Neg.	— —	— —	None	4 rays	Recovery (Crisis)	Uneventful recovery. Discharged well 4-29.	12.
13.	L. M. 782596	28	F	White	4-9	4-12	Fair	LL	I	Neg.	— —	— —	None	2 days	Recovery (Crisis)	Discharged well 5-3.	13.
14.	M. A. 783416	50	M	White	4-20	4-21	Fair	LL	XXI	Neg.	— —	— —	None	3 days	Recovery (Crisis)	Discharged well 5-2.	14.
15.	M. McK. 783066	13	F	White	4-13	4-17	Fair	LL	?	Neg.	— —	— —	None	3 days	Recovery (Crisis)	Patient did not raise any sputum. Patient developed rubella during convalescence. Discharged well 5-10.	15.
16.	J. G. 783653	50	F	White	4-18	4-23	Poor	RL, RM, RU	IX	Neg.	— —	— —	None	3 days	Recovery (Crisis)	Uneventful convalescence.	16.
17.	W. S. 784460	38	M	Col.	4-26	4-30	Fair	RL, RM RU	I	Neg.	— —	±	None	8 days	Recovery (Lysis)	Normal convalescence.	17.
18.	L. G. 784597	40	F	White	4-27	5-1	Poor	LU, LL	III	Neg.	— —	— —	None	2 days	Recovery (Crisis)	Crisis on second night in hospital; rapid and uncomplicated recovery.	18.

a. Streptococcus viridans, probably from saliva rather than sputum.
b. Sputum showed b. influenza and staphylococcus aureus.

Thus, despite the ever-increasing use of serum, and the advent of other newer methods of treatment, such as the oxygen tent, the death-rate from lobar pneumonia is essentially what it was a generation ago. Over a quarter of the patients admitted to a general hospital with this disease do not recover.

We come, therefore, more and more to the realization that in this disease symptomatic treatment is more important than specific treatment. In so doing, we go back to the conception of self-limited diseases voiced exactly one hundred years ago by Jacob Bigelow in a notable address delivered before the Massachusetts Medical Society[11].

Lobar pneumonia is a self-limited disease. If during its course we can promote rest and relaxation, if we can make the patient comfortable, ease the pain, relieve the dyspnea, lessen the apprehension, or if, in other words, we can help carry the patient along until such time as the illness has run its course, we shall have done the most valuable thing we can do in any self-limited disease. We feel that if the mortality of lobar pneumonia is ever lowered, it will be as a result of treatment directed along these lines, rather than as a result of any more specific treatment.

We do not imply that serum, for instance, has no value; even in our present small series of cases, several patients seemed to improve markedly after receiving it. The fact remains, however, that in any large series of cases, the mortality is about what it was before serum was used. There is beyond question a growing feeling that specific therapy is not so valuable as it appeared to be at first[12].

From our present series it is hardly possible to draw any definite conclusions. The number of cases is so small that statistics especially must be regarded with suspicion, and we feel that our results are suggestive rather than conclusive.

The mortality for the entire series is 22.2 per cent, not far from the figure that to date has appeared to be an irreducible minimum. It so happens that the mortality in the diathermy group is one-third that of the control group. Because of this, and because of the very definite subjective improvement in the patients treated by this method, we feel justified in continuing with this form of treatment until a sufficiently large series of cases, with controls, has been accumulated, and more definite conclusions may be drawn.

SUMMARY

A series of thirty-six consecutive cases of lobar pneumonia were given the standard treatment for this disease, including serum and/or oxygen when indicated. In addition, one half of the patients, alternately chosen, were given physiotherapy in the form of diathermy.

The mortality for the entire series was 22.2 per cent; that of the diathermy group 11.1 per cent, and that of the control group 33.3 per cent.

The cases are presented in some detail, and the effects of diathermy noted.

CONCLUSIONS

The use of diathermy is a valuable measure in the symptomatic treatment of lobar pneumonia.

It adds greatly to the comfort of the patient.

It appears to lower the mortality, although the present series of cases is too small to permit drawing any definite conclusions in this respect.

Further use of diathermy is indicated in this disease.

ACKNOWLEDGMENT: We wish to express our thanks to Miss Ruth Holmes, R.N., and to other members of the technical staff of the Physiotherapy Department of the Boston City Hospital, whose coöperation did much to make this study possible.

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SPECIFIC AND NONSPECIFIC ARTHRITIS*

(With Special Reference to Trauma)

BY BENJAMIN H. ARCHER, M.D.†

NUMEROUS attempts have been made to classify chronic arthritis. None have met with general acceptance. In part, this has been due to a lack of uniformity in nomenclature, and in part to gaps in our knowledge of the underlying cause.

For many years the pathologic condition and roentgenographic appearance of the joints have served as a basis for distinguishing the various types of arthritis. More recently the trend has been toward an etiologic classification[1].

Etiologically, chronic joint disease may be divided into two categories. In the first, the primary cause of the arthritis is known. In the second, the exciting agent of the disease is yet to be determined.

SPECIFIC ARTHRITIS

Exemplifying the first group are those cases of arthritis associated with specific infectious agents such as the gonococcus, the tubercle bacillus or the spirochaete pallidum. In addition, there are certain specific diseases which produce a chronic arthritis in which infection is not the primary cause. Syringomyelia, hemophilia, ochronosis and gout are examples of this group.

In syringomyelia the arthritis is probably due to a neurotrophic disturbance of the joints. The arthritis of gout and ochronosis result from the deposition of metabolic irritants in the joint cartilages. The joint changes of hemophilia are caused by the effusion of blood into the articular cavities.

In brief, it is quite clear that there are certain infectious and noninfectious diseases with known primary irritants that may result in chronic arthritis. To this type of case, it seems proper to apply the term, chronic specific arthritis. Furthermore, the group as a whole may be sharply defined, etiologically, from those instances of chronic arthritis in which the primary cause is unknown. The latter may be described as chronic nonspecific arthritis[2].

NONSPECIFIC ARTHRITIS

This would seem to be a good generic term. It serves to focus our attention on the fact that the primary cause of this type of joint disease is unknown. What is more, as our knowledge increases, it may be possible to separate various groups from this category and place them under the heading of chronic specific arthritis.

Pathologically, the joint lesions of nonspecific arthritis, like those of the specific form, fall into two groups. The terminology adopted by Nichols and Richardson[3] has much to commend it, and will be used throughout this article.

These authors divide the joint lesions of all forms of chronic arthritis into proliferative and degenerative types[4]. The first is characterized by primary proliferative changes in the synovial membrane and the perichondrium; the second by primary rarefaction and fibrillation of the central part of the articular cartilage.

It is important to remember that Nichols and Richardson in their classic monograph[3] emphasized the fact that their classification was purely a pathologic one and did not correspond to different etiological agents.

There is a striking similarity between the pathologic lesions of specific and nonspecific arthritis. This has led many investigators to suspect that both forms of chronic joint disease might be due to the same type of primary agents. With this in mind, intensive investigations have been carried out to find a specific bacterial agent, some neurotrophic disturbance or some abnormal concentration of metabolites in the blood, to explain the causation of nonspecific arthritis. As yet, there is no conclusive evidence at hand that any of these factors play a primary rôle in the etiology of this form of the disease[2].

Within recent years trauma has been reëmphasized as a primary cause of the degenerative type of nonspecific arthritis, and it is with this etiologic agent that we are specially concerned in this article.

TRAUMA

The relationship of trauma to chronic arthritis has been noted by many investigators. Nichols and Richardson[3] state that trauma may be one of the causes of either proliferative or degenerative arthritis. Leriche[5] describes "traumatic vasomotor synovitis". Leriche and Policard[6] believe that many injuries of the joints are followed by serious vasomotor disturbances of the fibrous tissue which may induce a proliferative arthritis. Büdinger[7], as early as 1908, reported splitting of the cartilage and thickening of the synovial membrane in cases of monarticular arthritis following trauma. He concluded that traumatic splitting of the cartilage is the most frequent injury of the knee joint, and

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that while many cases heal spontaneously, in a certain percentage an arthritis develops. Ludloff[8], Axhausen[9], Löwen[10], Kulowski[11], König[12] and Key[13] have substantiated Büdinger's conclusions.

All of these authors have discussed acute trauma of external origin, and have described the relationship of this irritant to the pathogenesis of the monarticular forms of arthritis.

The relationship of repeated trauma of intrinsic origin to the monarticular and polyarticular forms of chronic arthritis has been studied by other observers.

Miller[14] and Keefer[15] cite numerous examples of monarticular osteoarthritis due to repeated trauma. Heiss[16] has demonstrated the presence of this condition in Olympic athletes. Radiographic evidence of osteoarthritis was found in twenty-three of 159 men examined. In the football players the osteophytes were found principally in the knee; in boxers in the elbow or wrists, and in javelin and discus throwers in the elbow or shoulders. The primary cause of the arthritis in all these cases would appear to be repeated intraärticular trauma due to the excessive use of one or more joints.

Putti[17] believes that regardless of what the primary cause of multiple osteoarthritis may be, there always enters into its pathogenesis the factor of trauma; not the direct type, but that of the chronic type of moderate degree of intensity which occurs under various circumstances. Goldthwait, Painter and Osgood[18] state it is certainly true that continued strain or injury lead to the development of the hypertrophic type of nontuberculous joint disease (osteoarthritis). Henderson and Hench[19] are of the opinion that chronic forms of trauma result from the intrinsic causes of obesity and faulty posture and affect only the weight-bearing joints. Keefer and Myers[20] believe that the anatomic changes of osteoarthritis can be explained on a basis of injury to the cartilage and bone which follows the "wear and tear" upon joint structures. They stress the factors of senescence, occupational strain, and static abnormalities, as predisposing to the pathogenesis of the disease. Bauer[18] is in essential agreement with Keefer and Myers, and states, that degenerative osteoarthritis is the result of the "wear and tear" of increasing age and repeated trauma. Smith-Petersen[21], among others, has shown histologically the effect of multiple minimal traumata on joint surfaces. It was found that the microscopic changes were those of a degenerative arthritis.

From this brief review of the literature, one is apt to conclude that repeated trauma is a competent producing cause of the degenerative form of nonspecific arthritis. I believe this to be true, but I also hold that repeated trauma may produce proliferative arthritis. What is more, I believe that repeated trauma is not the sole cause of degenerative arthritis; there may be other causes, such as infection, metabolic irritants, vascular and neurotrophic disturbances. In the specific form of chronic arthritis this is quite obviously true, particularly in gout, syringomyelia, and congenital syphilis. In the nonspecific group, further investigation may reveal such irritants.

However, the importance of repeated intraärticular trauma as a factor in the causation of chronic arthritis of all types needs to be emphasized.

Repeated intraärticular trauma may be defined as continual abnormal pressure or friction upon the articular surfaces or synovial membrane of a joint. Normally there is pressure and friction upon these tissues. Pressure is due to the apposition of articular surfaces when at rest, and friction arises on motion. Under normal conditions, the cushioning effect of cartilage and the lubricating character of the synovial fluid seem to absorb the effect of friction on joint surfaces. Abnormal pressure or friction may result from any cause which disturbs the anatomic relationship of the joint surfaces or its enveloping membrane. It may also arise from excessive or abnormal use of a joint.

The chief predisposing causes of intraärticular trauma may be enumerated as follows:

1. Fractures of long bones near joints with faulty alignment of the fragments.
2. Intraärticular fractures and unreduced dislocations.
3. Foreign bodies in the joints.
4. Occupational or athletic stress and strain.
5. Constitutional causes, i.e., overweight, postural abnormalities, orthopedic disabilities and senescence.

In view of the number of causes that may produce repeated intraärticular trauma, there seems to be no valid reason for stressing senescence[22]. Senescence, as such, is not the cause of degenerative arthritis. It is repeated intraärticular trauma extending over a long period of years that is one of the primary agents of the joint changes seen in elderly people. Senescence is only a predisposing cause like overweight, orthopedic disabilities or postural abnormalities. The common denominator of all these constitutional causes of degenerative arthritis is repeated intraärticular trauma.

The mechanical theory of the causation of degenerative changes in the central part of the articular cartilage can be based on the fact that when fractured at right angles to its surface, articular cartilage presents a very definite striation (Fisher). It is quite reasonable to believe that abnormal pressure or friction at one point of the articular surface may cause in time a solution of continuity at that point. Repeated pressure or friction if prolonged at that point may result in a vertical splitting or cracking of the cartilage below the surface. This produces

so-called fibrillation or crevassing of the cartilage. The same process may occur at various points of the joint surfaces. This solution in continuity of the normal contour of the articular cartilage can result from abnormal pressure suddenly applied, as in acute external trauma, or may follow repeated small traumata intraärticular in origin. Weight-bearing and joint motion may then provide the force which eventually cracks the cartilage. The nature of hyaline cartilage with its semisolid consistency lends itself to this type of pathological reaction.

It is quite likely that any irritant which is able to disrupt the continuity of the surface of the central area of the articular cartilage may initiate degenerative pathological changes in this tissue. In addition to the mechanical causes which have already been enumerated, it is highly probable that any factor which diminishes the lubrication of the joint surfaces through interference with the production of mucin, may also lead to intraärticular trauma and erosion of joint surfaces.

It is important to remember that repeated intraärticular trauma may result in proliferative as well as degenerative changes in the joints. This is clearly evident in the action of foreign bodies on synovial membrane and articular cartilage. It is a well-known fact that a ruptured semilunar cartilage of the knee, in time, produces erosion of joint surfaces and degenerative osteoarthritis[23]. It needs to be emphasized that a foreign body in the same joint may result in a proliferative arthritis.

This has been demonstrated in osteochondritis dissecans[24]. In this disease, an aseptic necrosis of the articular cartilage results in the presence of a foreign osseocartilaginous body in the knee-joint. Because of repeated intraärticular trauma, the synovial membrane proliferates and a nonspecific arthritis follows.

Conway[24a] operated upon six such cases and reported that the changes in the synovia varied from a simple edema of the synovial papillae to a pronounced hypertrophy of the whole membrane. In one case, of long duration, he noted in addition to the proliferative changes, evidence of a degenerative arthritis.

Quite definitely, then, it may be stated that the same primary agent, repeated intraärticular trauma, may result in either a proliferative or a degenerative arthritis, depending upon whether the synovial membrane or the articular cartilage is principally affected by this irritant. What is more, if the irritation is sufficiently prolonged, inspection of the lesion may disclose both types of pathologic change in the same joint.

A survey of the literature and my own observations lead me to the following conclusions in regard to intraärticular trauma.

1. Repeated intraärticular trauma is a competent producing cause of some cases of chronic nonspecific arthritis.
2. Repeated intraärticular trauma may result in proliferative or degenerative pathologic changes in a joint, depending upon whether the synovial membrane or the articular cartilage is primarily affected by this irritant.
3. This form of trauma helps to explain the pathogenesis of degenerative arthritis in gout, ochronosis and hemophilia. It also explains the evolution of proliferative arthritis in osteochondritis dissecans.
4. Constitutional conditions may predispose to intraärticular trauma.
5. Occupational or athletic activity in which a single joint is used to an abnormal extent, sets up intraärticular trauma, and the result may be a degenerative arthritis at any age.
6. Acute external trauma that injures a joint may be a predisposing cause of repeated intraärticular trauma. The initial injury, which acute trauma may cause to the central part of the cartilage or to the synovial membrane, may in turn produce repeated intraärticular trauma. The latter may then become the primary agent of a chronic arthritis of the joint affected.
7. Any factor which diminishes the lubricating power of the synovial fluid predisposes to intraärticular trauma, by increasing the friction and pressure of joint surfaces.
8. Repeated intraärticular trauma is a primary cause of some cases of chronic nonspecific arthritis. It is a secondary factor in all types of chronic arthritis, specific and nonspecific.
9. No matter what the primary cause of an individual case of chronic arthritis may be, repeated intraärticular trauma tends to perpetuate the disease.
10. Even when the primary cause of a case of chronic arthritis is removed, the repeated intraärticular trauma which results from the derangement of the joint structure continues to act and may perpetuate the disease.

One cannot deny the importance of trauma in the causation and pathogenesis of chronic arthritis. Nevertheless, one must not overemphasize the rôle that this factor plays in the etiology of chronic joint disease.

Recently Bauer[18] has stated that degenerative osteoarthritis is the result of repeated trauma and senility. Keefer[18] maintains that all instances of degenerative osteoarthritis are the result of repeated trauma.

One immediately thinks of the degenerative joint lesions of syringomyelia and syphilitic osteochondritis as militating against this assumption[25]. What is more, degenerative osteoarthritis has been produced experimentally by the ligation of the blood-supply to the patella[26].

It is difficult to reconcile such evidence with the view that repeated trauma is the sole cause of osteoarthritis. Then again, as already noted, repeated intraärticular trauma may result in a proliferative arthritis. This irritant is therefore not a specific cause for a specific type of pathologic change in the joints. Finally, the characteristic lesion of degenerative osteoarthritis, the Heberden's node, cannot be explained on the basis of this theory.

It is quite obvious that the knuckle-joints and the proximal phalangeal joints are flexed and extended more frequently than the distal phalangeal joints. Indeed, it is well to recall, that because of the anatomic arrangement of the tendons of the fingers, most people cannot flex or extend the distal phalangeal joints without flexing and extending the proximal phalangeal joints[27]. It follows, then, that both of these joints are subjected to the same degree of repeated intraärticular trauma. Yet Heberden's nodes are a rarity in the proximal phalangeal joints and occur almost exclusively in the distal phalangeal joints[28]. Apparently some other factor or factors, besides trauma, must be operative, to explain the distribution of this lesion.

Though repeated intraärticular trauma is apparently not the sole factor in the etiology of all cases of degenerative arthritis, and indeed, may be a primary cause of some instances of proliferative arthritis, the important fact which must be borne in mind is that this irritant may be a secondary factor in every case of chronic joint disease.

CONCLUSIONS

1. Etiologically chronic joint disease may be divided into the specific and nonspecific forms of arthritis.

2. Intraärticular trauma may result from a number of diverse mechanical causes, i.e., fractures and dislocations, occupational or athletic activity, foreign bodies in the joints, and constitutional conditions.

3. Repeated intraärticular trauma may be the primary cause of some cases of chronic arthritis. It is a secondary factor in every case of chronic joint disease.

4. No matter what the primary cause of a case of chronic arthritis may be, repeated intraärticular trauma through friction or pressure tends to perpetuate the disease.

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GONADOTROPIC HORMONE (PROLAN) IN RELATION TO CARCINOMA OF THE CERVIX*

BY JAMES A. HALSTED, M.D.†

THE discovery in 1926 by P. E. Smith and Zondek and Aschheim, independently, that pituitary implants would activate the ovaries of immature rodents led to the demonstration of a substance in the urine of pregnant women which at first seemed to act similarly. This substance is the basis for the universally used test for pregnancy. Since this discovery the urine has been tested for it in a wide variety of conditions, among them cancer[1, 2].

Recently it has been clearly demonstrated by detailed biological tests that the pituitary hormone and pregnancy urine hormone are different substances[3, 4, 5]. Since they are both ovary stimulators it is well to speak of them collectively as gonadotropic substances and to differentiate them as the anterior pituitary hormone and the anterior pituitary-like hormone (A. P. L.—Collip). In all probability the hormone found in pregnancy urine (A. P. L.) is made by chorionic tissue. The same hormone is found in the urine of patients with hydatidiform mole and chorio-epithelioma.

In these three conditions large amounts of A. P. L. are excreted so that even if unconcentrated urine is injected into immature rodents ovarian changes will result, consisting of ripening of Graafian follicles (Prolan A effect-Zondek) and corpus luteum formation (Prolan B effect). Zondek first found gonadotropic substance in the urine in teratoma of the testicle, an embryonic tumor, and Ferguson[6] has shown that measurement of the hormone in the urine is of distinct aid in the management of these cases. Here the amount excreted is relatively small compared with the other conditions just mentioned, so that in many cases only by concentrating the hormone with alcohol can it be detected. This is Zondek's method for testing for gonadotropic substances in conditions other than pregnancy and chorio-epithelioma.

Anterior pituitary hormone is rarely found in this laboratory in the urine of "normal" women[7]. A positive test by Zondek's method thus constitutes an increased amount. The commonest cause of increased excretion is ovarian deficiency. Thus it is the rule to find it after removal of the ovaries, after the natural menopause has begun[8] and, as Österreicher[9] has shown, in many old women after the menopause is over. This is due to hyperfunction of the pituitary consequent to removal of the influence of the ovarian hormone. This explanation is supported by the experimental observations of Fichera[10] who noted an enlargement of the pituitary gland of rats after gonadectomy, and of Engle[11] who demonstrated an increased content of gonadotropic hormone in the pituitaries of castrated rats.

Zondek has tested for anterior pituitary hormone in the urine by the alcohol precipitation method in a large number of patients with various kinds of tumors and in 1930 reported the results of tests in fifty-five cases of genital carcinoma in women[1]. Forty of these cases were carcinoma of the cervix. He obtained positive tests in thirty-three and thence stated that 82 per cent of cases of carcinoma of the cervix were associated with positive tests. Because of the implication occasioned by this report that a positive test might be of significance in the diagnosis of carcinoma of the cervix, it was thought worthwhile to attempt to repeat his work.

Inasmuch as a positive test is to be expected in women with ovarian deficiency, patients with carcinoma of the cervix were selected who were under the menopause age and who had not been treated with radium or x-ray. Difficulty was experienced in finding a large number of such patients because most cases coming under observation had been treated previously or were beyond the menopause. Fifteen were studied during the course of the investigation, all of whom had normal menstrual histories prior to the onset of the disease. The diagnoses were all confirmed by histological section. One test for gonadotropic hormone was performed on each. The method used was essentially Zondek's method, mice being used as the test animals. Details of the test as performed in this laboratory are given by Albright, Halsted, and Cloney[7].

RESULTS

(See table.) Of the fifteen patients studied four or 26.6 per cent had positive tests. Two of these were forty-five and forty-seven years old and may have had relative ovarian deficiency in spite of normal periods. Occasionally a positive test has been obtained in this laboratory at the approach of the menopause before the periods have ceased. Eleven patients had negative tests. The table gives the pertinent data on each patient.

*The biological tests reported in this investigation were performed in the Biological Laboratory of the Massachusetts General Hospital under the direction of Dr. Fuller Albright. The expense was defrayed by a grant from the Delamar Mobile Research Fund.

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RESULTS OF TESTS FOR GONADOTROPIC HORMONE (PROLAN) IN 15 PATIENTS WITH CARCINOMA OF THE CERVIX

Case No.	Age	Duration of Disease	Menstrual History Before Disease Began	Gonadotropic Hormone Test
1. C. F.	36	3 months	Regular and normal	Negative
2. L. R.	44	3 months	Regular until 2 years ago. Since then irregular and profuse.	Negative
3. L. C.	27	3 years	Regular and normal	Negative
4. M. deL.	34	6 months	Normal until 1 year ago. Since then frequent and profuse.	Negative
5. C. C.	27	4 months	Regular and normal	Negative
6. M. S.	49	?	Regular and normal	Negative
7. D. C.	27	?	Regular and normal	Negative
8. D. C.	34	?	Regular and normal	Negative
9. F. B.	39	1 year	Regular and normal	Negative
10. L. C.	39	6 months	Regular and normal	Negative
11. I. L.	44	? 2 years	Regular and normal	Negative
12. A. D.	34	18 months	Regular and normal	Positive
13. M. W.	35	5 months	Regular and normal	Positive
14. G. P.	45	10 months	Regular and normal	Positive
15. C. R.	47	1 month	Regular and normal	Positive

Tests were performed on a number of patients with gynecological disorders suspected of being cancer which after operation turned out not to be. The negative tests were in two cases of endocervicitis, one of metropathia hemorrhagica and one of leiomyosarcoma. The positive tests were in one case each of chorio-epithelioma, endocervicitis, and cystic corpus luteum.

DISCUSSION

Zondek obtained positive tests in 82 per cent of his cases, and Saphir[2] in 80 per cent of five malignant tumors and 50 per cent of six benign tumors studied, whereas in this investigation positive tests were obtained in 26 per cent. However, on analyzing the data given for Zondek's cases one finds that many of his patients had either had previous radiation therapy, Wertheim operations (panhysterectomy with removal of both ovaries) or were at least fifty years old. Exact analysis of his data is impossible from the information given, but it is apparent that he obtained positive tests in only about half of his cases not suffering from ovarian deficiency. Saphir, unfortunately, does not mention the ages or menstrual histories of his patients.

Although one does not obtain positive tests in 26 per cent of normal women this relatively small percentage cannot be said to be of any significance in the diagnosis of carcinoma of the female genital tract. Whether it has any significance at all remains to be seen. Kurzrok[12] has demonstrated an increase of anterior pituitary hormone in the urine of ten women at the time of ovulation and believes it may be possible to determine the ovulation date by application of this test. Riley, Brickner and Kurzrok[13] obtained positive tests quite regularly before the headaches of patients with migraine. Smith and Rock[14] obtained positive tests in 45 per cent of cases of functional uterine bleeding. With the development of more refined methods for measuring the hormone in small amounts, it is probable that it will be found in more or less excess in a variety of conditions. It cannot be too strongly emphasized that methods for measuring gonadotropic hormone are most inadequate at the present time. The substance is apparently an unstable compound difficult to extract quantitatively and very divergent results have been obtained by equally competent workers. Only when very large amounts are being excreted, as in pregnancy and chorionic tumors, can much significance be attached to the result of a test.

SUMMARY

1. A brief account has been given of the various conditions which are known to be associated with an excess production of gonadotropic hormone (Prolan).

2. Although Zondek reported that 82 per cent of cases of carcinoma of the cervix had positive tests for gonadotropic hormone (meaning an increased amount) analysis of his cases shows that many of his patients had evidence of ovarian deficiency, in which condition a positive test is to be expected.

3. Twenty-six and six tenths per cent of fifteen patients studied in this clinic with carcinoma of the cervix and with normal menstrual periods prior to the onset of the disease had positive tests. This incidence which is, perhaps, greater than one would expect if there were not a relationship between cancer of the cervix and this hormone, still is not sufficient to be of diagnostic significance.

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MEDICAL PROGRESS

PROGRESS IN HEMATOLOGY*

(Late 1933 and 1934)

BY WILLIAM DAMESHEK, M.D.†

ADVANCE in hematology continues to be made along many fronts as interest in diseases of the blood-forming organs continues unabated. Many more workers are busy in this field, and the harvest of interesting and often important findings continues to be a rich one. Stress continues to be placed upon the physiological aspects of the various disease syndromes rather than upon the more purely morphological criteria which were the concern of the older hematologists. The most important advances have been in the field of etiology. The causes of pernicious anemia, chronic hypochromic anemia, congenital hemolytic anemia, and of agranulocytosis have been more clearly defined. No outstanding advance in therapy has been made, but then one cannot expect a liver announcement every year. The award of the Nobel prize in medicine to three Americans, G. H. Whipple, G. R. Minot, and W. P. Murphy, for their epoch-making work with liver emphasizes again the eminence of American hematology. The work of the Italian hematologists deserves more widespread attention than it has been given in this country, and the reviewer has been struck by the many comprehensive and excellently illustrated articles which have come out of the Italian clinics. The most notable text on hematology has appeared from Central Europe. It is the "Handbuch der allgemeinen Hämatologie" (Urban and Schwartzenberg, Berlin and Vienna, 1933) edited by Hans Hirschfeld and Anton Hittmair, and written by a large corps of specialists. Like many other ponderous German tomes, it is made up of two volumes and each volume is further divided into two halves (each of about 800 pages).

In last year's review (1929-1933), the approach was a general one with an attempt to present the subject of hematology in a broad way so that the reader might obtain a bird's-eye view of the field of hematology as it existed at the end of 1933. In the present review, more attention will be given to individual articles, although certain subjects will be stressed, i.e., anemia, agranulocytosis, glandular fever, and polycythemia.

THE BLOOD-FORMING ORGANS

The cells which circulate in the blood arise from three widely scattered centers of active cellular growth which have come to be called "organs". These are the bone-marrow, the lymphoid tissue, and the reticulo-endothelial system.

A. The Bone-Marrow. This, the most important of the blood-forming organs, is receiving increased attention as the result of recent studies. The sternal bone-marrow biopsy is receiving interested consideration. The sternum is easily entered by means of a hand trephine, a small plug of bone being obtained for sectioning and smears made on slides. Differential counts of the marrow in the sections have often proved of great diagnostic value. In the reviewer's hands, this procedure has proved of greatest value in the diagnosis of the often puzzling cases presenting chronic anemia, leukopenia, and thrombocytopenia, and has demonstrated that this triad of hematological signs is frequently due to aleukemic leukosis (q.v.).

B. The Lymphoid Tissue.

C. The Reticulo-Endothelial System. Great numbers of articles continue to be written about this important group of phagocytic cells which is scattered throughout the body but is found principally in the liver, the spleen, the lymph-nodes, and the bone-marrow. The reviewer has already cited the many activities of this "system" (*New Eng. J. Med.* 210: 531, 1934): the phagocytosis of foreign particles, the

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destruction of old red blood cells, the storage of fat, the formation of foreign body giant cells, the production of immune bodies, and the formation of the third type of white blood cells, the monocyte.

THE BLOOD CELLS

Terminology. For the red blood cells, terminology remains but little affected (cf. *New Eng. J. Med.* loc. cit.). The white blood cells have suffered some changes in terminology. Generally agreed upon are the following:

Bone-Marrow Cells: Myeloblast, Myelocyte, Metamyelocyte, Mature Polymorphonuclear cell. The metamyelocytes have been subdivided into "young" and "band" forms.

Lymphoid Cells: Lymphoblast, Lymphocytes, large and small. The "plasma" cell is a form of lymphocyte.

Reticulo-Endothelial Cells: Histiocyte, Monocyte. The word "monocyte" has come into general use and replaces the old term "transitional cell" as well as the ambiguous one of "large mononuclear cell".

The Polymorphonuclear Cells (Granulocytes). Schilling, following the lead of Arneth, subdivided the polymorphonuclear cells into myelocytes, young forms, band forms, and segmented (mature) forms. The value of this subdivision in the study of infectious disease has been adequately demonstrated in hosts of papers. As an example of carrying the method out to its logical conclusion may be cited the paper of Crocker and Valentine (*J. Lab. & Clin. Med.* **20**: 172, 1934). These authors have added a large number of new indices, the value of some of them being questionable. The introduction of mathematics into such a variable tissue as the blood does not have strict scientific backing, and although it is possible to sit in a laboratory and prognosticate with a fair degree of accuracy what is going on in a given case of infectious disease, it is sometimes of infinitely greater value to examine the patient. This should not detract, however, from any serious attempt to tabulate frequently exact findings in a given case of infectious disease and to interpret progress from them. The reviewer merely cautions against too literal an interpretation of hematological data in infectious disease since these data should simply be regarded as symptoms or signs in a complex which, in its entirety, represents a diagnostic or prognostic interpretation.

The Lymphocytes. Wiseman (*J. A. M. A.* **103**: 1524, 1934) discusses the origin, physiology, and morphology of the lymphocyte. He states that the lymphocyte has a "definitive" life cycle similar in all respects to that of the polymorphonuclear cell and the erythrocyte. (This is not new; hematological treatises for many years have differentiated primitive lymphocytes; large or immature lymphocytes often with dark blue cytoplasm; and small lymphocytes with pyknotic nuclei.) Wiseman points out that increased activity of lymphoid tissue is accompanied in the blood stream by increased numbers of lymphocytes with increased concentration of basophilic substance in the cytoplasm. (Cf. the findings in "glandular fever" q. v.) It is axiomatic that hyperplasia of any of the three blood-forming organs is reflected to greater or less degree in the peripheral blood. Arneth and now Wiseman suggest studying the lymphocytes for variations in immaturity; the reviewer has found careful studies of this type of value in glandular fever and lymphatic leukemia.

The Monocytes. The importance of the monocyte has loomed large in recent literature, chiefly because of its association with the reticulo-endothelial system, from which it is derived.

Wiseman in the above cited paper discusses the origin of the monocyte and its relationship to the "clasmatocyte" and demonstrates how knowledge regarding this cell has gradually been built up, particularly from the study of monocytic leukemia. The monocyte and the clasmatocyte are in all probability related cells, says Wiseman, since they appear together in experimental tuberculosis, and in the blood stream in monocytic leukemia. Levi and Penati in an extremely careful and complete piece of work (*Arch. per le Sc. med.*, **58**: 773, 1934) discuss the fundamental experimental and clinical data bearing on the origin of the monocytes. They produced experimental reticulo-endothelial reactions by the injection in animals of electro-negative colloids and studied the resultant blood-picture. Experimental monocytosis was also produced with the bacterium monocytogenes, various vaccines, and experimental tuberculosis. These authors point out that a reticulo-endothelial reaction in the tissues and monocytosis in the blood are not always correlated, and that it is possible to obtain a high grade of monocytosis without any hyperplasia of this system. They feel it is less difficult to derive the monocytes from the bone-marrow hemocytoblasts. In their second paper, Penati and Levi discuss clinical monocytosis and monocytopenia, infectious "mononucleosis", and monocytic leukemia in great detail, together with the bearing of these conditions upon the various theories regarding the origin of the monocytes. They conclude that the monocytes are derived from hemocytoblasts (usually myeloid, at times lymphoid in origin), and that the doctrine which derives these cells from the reticulo-endothelial system is not sufficiently documented. (Hemocytoblasts of the Ferrata type and histiocytes are in all probability synonymous terms. The sum-total of hemocytoblasts [histiocytes] found in the bone-marrow, spleen, liver, and lymph-nodes may be called the "reticulo-endothelial system".

There is in reality no strict divergence in views between the theory that the monocytes are derived from the cells of the reticulo-endothelial system and that which states that they originate from hemocytoblasts.)

Red Blood Cells. The *reticulocytes*, immature red blood cells, have continued to be of first importance in the study of the anemias, particularly from the therapeutic standpoint. Osgood and Wilhelm (*J. Lab. & Clin. Med.* **19**: 1129, 1934) state that the reticulocyte methods ordinarily in use give results which are too low. These investigators mix a small quantity of blood with brilliant cresyl blue in a test tube and then make smears. The normal percentage of reticulocytes by this method is frequently 2-4 per cent. Dameshek (*W. Virginia M. J.* **30**: 193, 1934) showed that the reticulocyte response in hypochromic anemia following the use of inorganic iron varied directly with the extent of reduction in hemoglobin. At a hemoglobin level of 20 per cent, the maximal reticulocyte response with the use of an optimal dose of iron was 10-15 per cent. Minot (*Tr. A. Am. Physicians* **49**: 287, 1934) indicated the value of the "double reticulocyte response" in the study of the therapeutic potency of various extracts of liver. Dameshek and Castle (*J. A. M. A.* **103**: 802, 1934) used this method in assaying the potency of various commercial extracts of liver for parenteral use in pernicious anemia. First one extract was injected and daily reticulocyte counts obtained; after a ten-day period of observation, another extract was given in the same dosage. If a second reticulocyte response occurred, the second extract was considered to be definitely more potent than the first.

The sedimentation rate of the red blood cells continues to be widely utilized. Cherry (*J. Lab. & Clin. Med.* **20**: 257, 1934) after a careful analysis of the various factors which influence the sedimentation rate, comes to some very sensible conclusions, to which the reviewer subscribes. Cherry states that "to rely upon this test, without other laboratory data, is unwise. . . . From a clinical point of view, the sedimentation test alone is confusing, because individuals react biochemically to disease in different ways, thereby producing variations in rate in the same pathologic state. As a prognostic aid it is of slight help. The leukocyte count or filament—non-filament study in conjunction with the clinical picture is of much greater aid than the sedimentation rate." So many articles are written which are enthusiastic about the outstanding value of the test in this field or that, that it is refreshing to read a critical article which places the test in its proper category: simply another symptom or sign (often misleading like other symptoms and signs) indicating an abnormal bodily state.

Stainsby (*M. Clin. N. Amer.* **18**: 911, 1934) in writing of the value of the sedimentation test discusses its value in the neuroses. It is sometimes difficult to make up one's mind whether the patient's complaints are on a "functional" basis or composed of more solid stuff. With an elevated rate, considerable effort should be made to determine the underlying morbid process. Stainsby adds, however, that a normal rate does not rule out organic disease. He points out the value of the procedure in following the course of rheumatoid arthritis and in indicating the end of the active process in rheumatic fever and pulmonary tuberculosis.

ANEMIA

Etiology. Some of the most important advances in our knowledge of anemia have been made in the understanding of the underlying etiological factors which are concerned. The bone-marrow, in which are formed all of the red blood cells, must be provided with a sufficient quantity of "liver substance" as Castle (*Ann. Int. Med.* **7**: 2, 1933) has pointed out. This depends upon (1) a diet adequate in vitamin B_2, protein, and iron; (2) a well-functioning gastric mucosa in which protein-splitting and iron-dissolving enzymes are present; and (3) a normally absorbing bowel.

The Diet. The importance of the diet, particularly its vitamin B content, previously stressed by Castle and Rhoads, was confirmed by Lucy Wills (*Lancet* **1**: 1172, 1934) in her studies of the "tropical macrocytic anemia" and the "pernicious anemia of pregnancy" seen in India. The most striking work indicating the correlation of the diet, particularly that containing vitamin B_2, with development of macrocytic anemia has been performed by Rhoads and Miller (*J. Exper. Med.* **58**: 585, 1933) on dogs. These investigators, by feeding dogs a diet inadequate in vitamin B_2 were able to produce glossitis, stomatitis, gastrointestinal disturbances such as diarrhea, severe macrocytic anemia, and a megaloblastic hyperplasia of the bone marrow typical of that of human pernicious anemia. This disorder, if not too severe, responded to vitamin B_2 containing preparations but not to parenteral liver extract, indicating a different type of absorption mechanism in the dog as compared with the human being.

Davidson and Leitch (*Nutrition Abstr. & Rev.* **3**: 901, 1934) take up in great detail the importance of a sufficient quantity of iron in the dietary, not only in human beings but in animals as well. They determined that "first-class animal protein" and green vegetables are deficient in the diets of the poorer classes and that these inadequacies may result in an iron-deficient anemia. The same mechanism holds

true in the nutritional or milk anemia of infancy, as pointed out by Josephs (*Bull. Johns Hopkins Hosp.* **55**: 259, 1934). This author demonstrated by careful metabolic studies that the "birth-stores" of iron derived from the mother were probably sufficient to last to the end of the sixth month under normal conditions. However, with a continued low iron diet, such as is found in an exclusive milk diet and possibly on account of other factors, microcytic hypochromic anemia due to iron deficiency would develop.

The Stomach. Castle's epoch-making contributions which indicated so strikingly how intimately the condition of the gastric mucosa was related to the normal hematopoietic function have been abundantly confirmed. Strauss (*J. A. M. A.* **103**: 1, 1934) reviewed the entire concept in an article on the rôle of the gastrointestinal tract in conditioning deficiency disease. Deficiency diseases, he brings out, are not only those in which a substance like vitamin B_2 is lacking from the dietary, but may develop when the substance enters the body but fails to reach the essential organs concerned. Pernicious anemia is a "conditioned" deficiency disease because the deficiency is caused not by a defective diet but usually by the absence from the gastric juice of a specific heat-labile factor (Castle's enzyme or "intrinsic substance"). (It must be remembered that many cases of pernicious anemia have a strong dietary factor as well as a gastric factor and the disease probably does not develop in these instances until the diet becomes poor.) Usually the cause for this loss of the specific enzyme from the stomach in a case of pernicious anemia is not clear but some cases develop following gastrectomy, polyposis of the stomach, and diffuse gastric carcinoma. Madelaine R. Brown (*New Eng. J. Med.* **210**: 473, 1934) investigated 151 autopsies of cases of undoubted pernicious anemia and found that eighty-two had gross lesions affecting the gastrointestinal tract. Forty-one of forty-two histological studies of the stomach showed chronic gastritis with or without a loss of glandular epithelium; and in thirty-seven the acidophilic cells had disappeared. She therefore concluded that achylia gastrica in pernicious anemia is due to a loss of acidophilic cells. Fouts, Helmer, and Zerfas (*Am. J. M. Sc.* **187**: 36, 1934) investigated the concept enunciated by Morris and his associates that pernicious anemia was due to the absence of a "hormone" from the gastric juice. They concluded on the basis of experiments with gastric juice kept at different temperatures for varying lengths of time, and from other experiments in which the various gastric enzymes were separated by ultrafiltration (*Am. J. M. Sc.* **188**: 184, 1934) that the reason for the ability of Morris's gastric juice concentrate to induce a remission in cases of pernicious anemia was on account of the interaction which took place between Castle's enzyme and the globulin of the gastric juice. (Castle has previously shown that normal gastric juice alone is not sufficient to stimulate hematopoiesis, but that an interaction between gastric juice and protein or vitamin B_2 was necessary.) It has thus been adequately demonstrated that the normal gastric juice contains an enzyme, which is not rennin or pepsin, the function of which is to interact with protein or vitamin B_2 containing foods. The resultant substance after absorption by the bowel stimulates or nourishes the bone-marrow so that normal red blood cell formation takes place.

It must not be supposed that the "intrinsic substance" of Castle is the only factor of importance in the gastric juice. The reviewer has suggested that the lack of hydrochloric acid in cases of chronic "primary" hypochromic anemia might be of causal importance in the disease. Mettier, Kellogg and Rinehart (*Am. J. M. Sc.* **186**: 694, 1933) in their study of ten cases came to the same conclusions, i.e., that the gastric dysfunction leads to failure in utilization of organic iron. This is also well brought out by the Italian investigators Allodi, Penati, and Quaglia (*Minerva Med.* **25**: 489, 1934). It is likely that the hydrochloric acid of the gastric juice aids in the preliminary solution and digestion of organic iron. Its continued absence, possibly in the presence of other factors (dietary, hemorrhagic, etc.) leads gradually to an iron deficient state, i.e., hypochromic anemia.

The Intestines. That a normally functioning bowel is essential in the absorption of the hematopoietic stimulants formed in the stomach had already been postulated by Castle (*Ann. Int. Med.* **7**: 2, 1933). Strauss points out (*J. A. M. A.* **103**: 1, 1934) that macrocytic anemia indistinguishable from pernicious anemia may develop in the presence of various types of intestinal lesions such as celiac disease, idiopathic steatorrhea, and chronic stricture of the bowel. Hare (*Brit. M. J.* **2**: 162, 1934) concluded that ulcerative colitis may bring about various types of anemia, whether macrocytic, microcytic, or a combination of both. That the gastric lesion in pernicious anemia may not be the only one present was commented upon by Madelaine Brown (*New Eng. J. Med.* **210**: 473, 1934) who found that lesions of the intestines with enteritis were frequently present. It may thus be seen that anemia may develop (1) as the result of a diet deficient in (a) protein, (b) iron, (c) vitamin B; (2) as the result of some gastric defect; (3) as the result of some intestinal lesion. The latter two mechanisms are important in the development of the "conditioned" deficiency diseases among which pernicious anemia, primary hypochromic anemia, and pellagra are prominent.

OTHER FACTORS

The Liver. Recent investigations have demonstrated that the liver is important in normal

hematopoiesis. This had been suspected since Whipple, Minot and Murphy's epoch-making investigations of the efficacy of liver in the treatment of anemia. Wintrobe and Shumacker (*Bull. Johns Hopkins Hosp.* **52**: 387, 1933) on the basis of three cases of macrocytic anemia associated with disease of the liver suggested that the liver stores and possibly elaborates to some extent the hematopoietic principle produced by the interaction of the intrinsic and extrinsic factors of Castle. Other authors such as Van Duyn (*Arch. Int. Med.* **52**: 839, 1933) and Heath (*Folia Haemat.* **51**: 391, 1934) have taken up this attractive hypothesis. Heath states that the anemia in cases of hepatic cirrhosis is probably explainable on the basis of a loss on the part of the liver of the capacity of providing sufficient of the needed material for normal red cell formation. Goldhamer, Isaacs, and Sturgis (*Am. J. M. Sc.* **188**: 193, 1934) make an important contribution to this problem. By making extracts of human liver derived respectively from a fetus, an inadequately treated case of pernicious anemia, an adequately treated case, a case of cirrhosis of the liver, and a case of acute yellow atrophy of the liver and then giving them parenterally to patients with pernicious anemia, these investigators were able to demonstrate that the liver is probably a storage reservoir for "active principle". The anemia of cirrhosis of the liver may be due, these authors state, to failure of normal hematopoiesis to take place. These speculations, although attractive, probably do not give the entire explanation. It is likely that severe liver damage may be a factor in certain cases of anemia, but it is also probable that other factors must be present as well, such as an inadequate diet and an impaired gastrointestinal tract.

The importance of *pregnancy* as a factor in the development of anemia has been studied by Strauss (*J. A. M. A.* **102**: 281, 1934) who postulates that the fetus removes from the mother a definite store of "active principle" and of iron. In the presence of achlorhydria, the mother may be said to be vulnerable and unable to keep pace with this continued loss of substance to the fetus, and anemia may develop. Dieckmann and Wegner (*Arch. Int. Med.* **53**: 188, 345, 1934) have studied the blood of a group of normal pregnant women with great care and have demonstrated that anemia of a mild type develops in most of them, the anemia being most marked between the twenty-sixth and the thirty-fifth week.

The constitutional or hereditary factor probably plays some part, principally in pernicious anemia, possibly as well in primary hypochromic anemia. This was recently emphasized by Friedlander (*Am. J. M. Sc.* **187**: 634, 1934) who studied 500 cases of pernicious anemia. This disease, which is largely confined to the white race in temperate zones, is present particularly in "those individuals endowed with a diathesis characterized by a fair complexion, light hair, blue eyes, and achlorhydria".

METHODS OF STUDY

Hemoglobin. The reviewer has already noted the tendency in recent years to record hemoglobin in grams per 100 cc. of blood rather than in per cent of normal. What is supposed to be normal has varied from method to method; it may be 13.8 by one method and 17.2 Gm. per 100 cc. by another. The Tallqvist and Dare methods have been found unacceptable by the reviewer and by Dieckmann and Wagner (*Arch. Int. Med.* **53**: 188, 1934); the latter investigators also found the Sahli method unreliable, although if it is done with due care and if the tubes and standards are calibrated against the Van Slyke oxygen capacity method, it will be found to be satisfactory for clinical use. The Newcomer method although seemingly more accurate may be unreliable at low readings. Dieckmann and Wagner have found the Haldane-Palmer carboxyhemoglobin method most satisfactory. The reviewer is becoming more and more convinced that determination of the hemoglobin indirectly by determination of the blood iron should have far wider use (cf. Peters and Van Slyke; the Wong iron method). Sachs, Levine and Appelsis (*Arch. Int. Med.* **52**: 366, 1933) found that the average iron content of whole blood of 100 normal men was 50.01 mgs. per 100 cc., that of women definitely less. The iron content is roughly 0.3 per cent of the total hemoglobin.

Mean Corpuscular Volume. Wintrobe (*Am. J. M. Sc.* **185**: 58, 1933 and *Arch. Int. Med.* **54**: 256, 1934), Heath (*New. Eng. J. Med.* **209**: 173, 1933) and many others have demonstrated that determination of the average volume of the red blood cell is an important diagnostic procedure, particularly in the diagnosis of the macrocytic anemias. The mean corpuscular volume is determined by first obtaining the volume of packed red blood cells per unit of blood. This may conveniently be done by centrifuging the blood in a Wintrobe 1 cc. hematocrit tube (the blood is prevented from clotting by the use of dry sodium oxalate) and observing the volume of packed red blood cells. This figure per 1,000 cc. of blood (normally 460) is divided by the erythrocyte count in millions, the resultant figure being the mean or average corpuscular volume in cubic micra. Examples: (1) Hematocrit (volume of packed red cells per 100 cc. of blood) 46; R.B.C. 5.0 millions; M.C.V. $\frac{46 \times 10}{5.0} = 92$. (2) Hematocrit 40; R.B.C. 3.0 millions; M.C.V. $\frac{40 \times 10}{3.0} = 133$. Wintrobe gives the following figures: normal or normocytic 84-92; macrocytic, greater than 94; microcytic, less than 80 cubic micra.

Red Blood Cell Diameter. Janet M. Vaughan and Helen M. Goddard (*Lancet* 1: 513, 1934) compared the results obtained by mean corpuscular determinations with those obtained by determining the average cell diameters and concluded that volume can be regarded as a measure of cell size in pernicious anemia and in primary hypochromic anemia but that there were occasional discrepancies as in congenital hemolytic anemia when the red cells are unusually thick and in certain other cases. The reviewer has found both methods to be of value, although the determination of the corpuscular volume is less time-consuming and laborious. The occasional discrepancies should be checked by careful examination of the stained blood smear.

CLASSIFICATION

The tendency in recent years has been to escape from the greatly involved often meaningless classifications of the past and to substitute for them a simple classification based on cell size or volume. Wintrobe (*Arch. Int. Med.* 54:256, 1934) is one of the foremost exponents of this view, to which the reviewer heartily subscribes. Roughly, all cases of anemia may be classified as macrocytic, normocytic, and microcytic. The macrocytic (large cell) anemias, Wintrobe brings out, are characterized by an increase in the average red blood cell diameter to 8.0-8.5 micra and an increase in the mean corpuscular volume to above 94 cubic micra. The normocytic anemias have a normal red cell diameter (7.0-7.5 micra) and a normal average red cell volume (80-94). The microcytic anemias, which are usually hypochromic as well, are characterized by small average cell diameter (6.0-6.5 micra) and a low average red cell diameter (less than 80 cubic micra). The most common of the macrocytic anemias is "pernicious anemia", but many other types are present associated usually with a deficiency in Castle's antianemic principle (see Etiology). Normocytic anemia is usually associated with decreased bone marrow function (aplasia, hypoplasia). Microcytic anemia is associated with a deficiency in iron from the body and is seen particularly in chronic blood loss and in the chronic hypochromic anemia of middle-aged women with achlorhydria.

The above terms should be qualified by indicating the possible etiological factors present: thus

Macrocytic anemia: poor dietary, achlorhydria, diarrhea
Normocytic anemia: benzol
Microcytic anemia: achlorhydria, pregnancy.

PERNICIOUS ANEMIA

Some of the most important advances in the past few years have been made from the standpoint of etiology (q.v.). The concept is gradually becoming established, as enunciated by Castle (*Ann. Int. Med.* 7: 2, 1933) that pernicious anemia is not in reality a separate disease, but rather the end-result of many diverse factors, whether dietary, gastric, intestinal, or hepatic in origin. The end-result is a megaloblastic marrow with the resultant presence in the peripheral blood of macrocytes. It is important therefore in every case of suspected pernicious anemia to study very carefully the gastrointestinal tract and the diet.

Diagnosis. It has struck many students of the disease that outspoken cases are on the decrease and that most instances are relatively mild so far as the anemia goes, although the neurological symptoms may dominate the picture. McGhie (*Canad. M. A. J.* 30: 274, 1934) makes a plea for early diagnosis and stresses such symptoms as anorexia, sore tongue, paresthesias, and difficulty in locomotion, together with such signs as glossitis, diminished vibratory sensation, and increased reflexes. Neurasthenia, arthritis, some gastrointestinal disorder are all apt to be diagnosed unless one takes pains to do very careful hematological work in these patients. Early examples of "combined system disease", which is in reality part and parcel of the greater syndrome of pernicious anemia, are often associated with what at first glance is an almost normal blood picture. However, careful investigation will usually show the following: slight reduction in red blood cells (3.5 to 4.0 millions), high color and volume index, increased mean corpuscular volume, low white blood cell count, macrocytes with an increase in the average diameter of the red cells, presence of "pernicious anemia neutrophiles", slight increase in icterus index and in bilirubin content of the blood, and complete achlorhydria. Wintrobe has pointed out (*Arch. Int. Med.* 54: 256, 1934) that the mean corpuscular volume is of utmost importance in diagnosis. The color index, depending as it does upon an accurate hemoglobin determination and an accurate erythrocyte count, is very frequently in error, but the corpuscular volume is easily obtained when the hematocrit determination and the red cell count are known. In making a diagnosis it is futile to wait until severe anemia is present and nucleated red blood cells are present in the smear. In the presence of (1) the findings indicating macrocytosis, (2) glossitis, (3) achlorhydria after histamine, and (4) neurological changes usually of posterior and lateral column involvement, the diagnosis of pernicious anemia is justified. The reviewer has frequently pointed out that certain cases of aleukemic leukosis will simulate very closely all of the hematological features of pernicious anemia. With the presence of splenomegaly, and particularly when therapeutic response to liver extract does not take place, this possibility

should be suspected. It is important above all else in any case presenting neurological lesions particularly those of the extremities to rule out pernicious anemia, since treatment in the latter event may be so effective.

Treatment. Advance in the therapy of pernicious anemia continues unabated. Dameshek and Castle (*J. A. M. A.* **103**: 802, 1934) state that liver from the cow, the pig, the horse, even the codfish has been utilized and has been given in the form of a powder for oral use and in solution for parenteral administration. These authors state that parenterally given (intramuscular) solution of liver extract has been demonstrated to be 30 to 100 times as effective as orally administered extract. Thus the material derived from 100 Gm. of liver (if fully potent) when given intramuscularly is equivalent to 3,000 to 10,000 Gm. of material given orally. There is, to be sure, some loss in potency in too great a "refinement" of extract, particularly when it is "concentrated" in small bulk. However, even with this loss of potency a large amount of effective material is introduced when 3 cc. of solution containing the material derived from 100 Gm. of liver extract is given intramuscularly. This is particularly valuable when the central nervous system is involved, and has completely modified the prognosis for these cases. Striking responses are often obtained with the persistent and extremely frequent use of the "concentrated" products of liver extract. When faced with a case of this type, it is the custom of the reviewer to inject daily doses of the material derived from 100 cc. of extract in the deltoid or gluteal muscles until definite improvement begins. This is followed by doses given every two days, then every three days, and when the patient is ambulatory, once weekly or even every two weeks. Some patients require weekly doses, others bi-weekly doses in order to continue hematologically normal (5.0 million r.b.c.) and neurologically relatively free of symptoms. Complete cure of the neurological symptoms is to be expected only in the mild cases showing paresthesias and slight to moderate loss in vibratory sense. In those patients presenting spasticity and ataxia, 50 to 75 per cent improvement in gait and in strength can be expected, although the reflex changes will persist almost unchanged. Those cases with posterior column involvement alone usually do better than those with lateral column involvement as well. Striking, even unbelievable improvement sometimes occurs and is indeed a contrast even to the results obtained with oral liver therapy. Goldhamer, Bethel, Isaacs, and Sturgis (*J. A. M. A.* **103**: 1663, 1934) and Grinker and Kandel (*Arch. Int. Med.* **54**: 851, 1934) are, however, pessimistic regarding the effects of therapy.

The exact therapeutic effect of vitamin B containing products is still uncertain. Davidson (*Brit. M. J.* **2**: 481, 1933) reviewed the therapeutic effects of yeast products in different types of anemia and concluded that some hematopoietic principal was present, although in small concentration. Lassen and Lassen (*Am. J. M. Sc.* **188**: 461, 1934) cite the conclusion of Strauss and Castle that the extrinsic factor "may now be defined as a substance closely related to vitamin B_2, if not vitamin B_2 itself". (Castle, in an editorial note in the same article, states that he is fully prepared, however, to relinquish this suggestion.) These authors concluded on the basis of careful experimental work that the "extrinsic factor searched for by Castle is not identical with vitamin B_2 nor with B_1, and presumably not with any other fraction of the vitamin B complex". It is difficult to explain the often striking results obtained in cases of pernicious anemia with "marmite" (an autolyzed yeast product), unless other substances, as Lucy Wills and Naiseh state (*Lancet* **1**: 1286, 1933), are present in this crude commercial product. Miller and Rhoads (*New Eng. J. Med.* **211**: 921, 1934) state that "conclusive proof of the identity or lack of identity of the dietary antianemia factor and vitamin B_2(G) clearly must be deferred until isolation of the vitamin in a pure form has been effected". This is a rather conservative conclusion since these authors demonstrated that a rice-polishings concentrate after incubation with normal gastric juice gave a clear-cut reticulocyte and erythrocyte response in a case of pernicious anemia.

PRIMARY HYPOCHROMIC ANEMIA (IDIOPATHIC HYPOCHROMIC ANEMIA; ACHYLIC CHLORANEMIA; ACHLORHYDRIC ANEMIA; HYPOFERRIC ANEMIA; CHRONIC HYPOFERRISM)

Various authors have confirmed the original findings of Kaznelson, Reimann, and Weiner, Dameshek, Witts, Davies, and others regarding the presence of a so-called "primary" anemia with a "secondary" type of blood-picture (i.e., low color index, achromia of the red cells, etc.). Mettier, Kellogg, and Rinehart (*Am. J. M. Sc.* **186**: 694, 1933) found that the food intake was frequently deficient in iron and that the gastric contents were almost always completely achlorhydric. Dameshek (*J. A. M. A.* **100**: 540, 1933) pointed out that the disease was in all probability a chronic iron deficiency state and that these symptoms of early greying of the hair, wrinkling of the skin, sores about the mouth, atrophy of the tongue, brittleness and flattening of the finger nails were probably "trophic" disturbances dependent upon a lack of iron in the bodily cells. A careful study of the disease was made by the Italian investigators Allodi, Penati, and Quaglia (*Minerva Med.* **25**: 489, 1934) who confirmed the above clinical findings and also expressed the view that the pathogenesis of the disorder was in great part linked up with a deficient function of the stomach. Recent studies have convinced the reviewer that most cases are associated with multiple etiological factors (as noted in chapter on Etiology). The diet is fre-

quently deficient, the gastric juice is defective, and often an added factor of bleeding (menorrhagia, from hemorrhoids, etc.) is present. Multiple pregnancies are also important in the pathogenesis of the disorder.

Treatment. The treatment of the condition, whatever the cause, is relatively simple. The body may be said to be in a state of iron starvation and large quantities of iron are necessary. Dameshek (*W. Virginia M. J.* **30**: 193, 1934) determined the optimal dosages of iron for various preparations to be as follows: *ferric ammonium citrate* 3.0 to 6.0 Gm. daily (given either in the form of 0.5 Gm. capsules, in 25 per cent solution or as the scale salt itself in 2 Gm. dosage dissolved in milk); *reduced iron* 3.0 Gm. daily (given in 0.5 to 1.0 Gm. capsules); *ferrous chloride-ferrous glutamate* 4 Gm. daily. In using these large doses of iron, it is wise to begin with a relatively small dose and accustom the patient's gastrointestinal tract to its presence; when this is done, the dose can gradually be raised to the optimal dosage. Recently, *ferrous salts* have been advocated as being superior in absorptive power and necessitating smaller doses of material. The reviewer has compared a ferrous compound with reduced iron and ferric and ammonium citrate and has found it to be at least as effective (ibid). Fullerton (*Edinburgh M. J.* **41**: 99, 1934) used ferrous sulphate and found that a small dose of the dried salt (0.8 Gm.) was as effective in hemoglobin regeneration as 6.0 Gm. of ferric ammonium citrate. The reviewer has pointed out in the above publications that most cases of hypochromic anemia will respond when adequate dosage of iron is given, but that an occasional case which is refractory responds when copper in the form of copper sulphate 0.006 Gm. is added to the daily iron ration. It is probably inadvisable to use copper except in the occasional refractory case, since chronic copper poisoning with possible hemochromatosis may result.

Organic compounds of iron are probably of little or no value, certainly as compared with the inorganic preparations. This is brought out in the experiments of Elvehjem, Hart, and Sherman (*J. Biol. Chem.* **103**: 61, 1933). Patek and Minot (*Am. J. M. Sc.* **188**: 206, 1934) made the interesting observation that concentrated bile pigment alone might increase the hemoglobin or might facilitate the absorption or utilization of iron. One patient, unable to obtain a normal hemoglobin level with large doses of iron, showed an increase in hemoglobin concentration when bile pigment was administered in addition to the iron.

OTHER TYPES OF ANEMIA

Aplastic Anemia. Thompson, Richter and Edsall (*Am. J. M. Sc.* **187**: 77, 1934) found, on analyzing a group of cases of aplastic anemia, that many discrepancies were present between the textbook description of the classical case and their cases as observed at the bedside. (This is probably true for many conditions.) They found that evidences of regeneration were frequently present. (On the other hand, careful analysis of their cases will show that certain of them were in all likelihood examples of aleukemic leukosis [q.v.].) The reviewer (*New Eng. J. Med.* **210**: 687, 1934) stated that although certain idiopathic cases of aplastic anemia are still encountered, the great majority present a more or less well-defined history of contact with a chemical such as benzol, arsenic, arsphenamine, neo-arsphenamine, radium, radioactive substances, mesothorium in watch-dial workers, x-rays, and gold. He reported a case following the use of large amounts of gold sodium thiosulphate in the treatment of lupus erythematosus. There has been no advance in therapy in this disease, the custom being to give numerous transfusions until further evidence of blood regeneration appears lacking. Gottlieb (*Ann. Int. Med.* **7**: 895, 1934) recommends trial of splenectomy and cites a case in which a remission occurred lasting for two months.

Congenital Hemolytic Anemia. The most striking advance in this disease has been the discovery that the fundamental abnormality is an increased tendency of the red blood cells to assume a spherical shape. Naegeli, in the last (1931) edition of his textbook and Haden (*Am. J. M. Sc.* **188**: 441, 1934) designate this tendency as spherocytosis. This abnormality was discovered by comparing the average red blood cell diameter which is always less than normal (microcytosis) with the average corpuscular volume, which may be normal or even increased. This can only be due to an increased thickness of the red cells, which Haden and Naegeli feel is an inborn error in the disease, as much of an anatomical variation as the "tower" skull and other physical abnormalities often present. Haden found that the increased fragility (the amount of dilution necessary to produce hemolysis) varied directly with the degree of spherocytosis or altered shape of the cells, and stated that "the cells in this disease may be regarded as nearer the hemolysis point by reason of their shape". He concludes that "the one fundamental variation from normal is the microspherocytosis. The anemia, jaundice, splenomegaly, reticulocytosis, and increased fragility are all secondary to the globular form of the erythrocyte".

As regards treatment, Reifenstein and Allen (*J. A. M. A.* **103**: 1668, 1934) recommend, on the basis of three cases, the use of parenteral liver extract, particularly in the mild case of the disorder. Their three cases all showed definite clinical improvement. Other observers dis-

agree with this concept, however, maintaining that not only may hemoclastic crises appear but that the gall-bladder and liver may become irretrievably damaged before splenectomy is finally done.

Ovalocytosis, Sicklemia, Sickle-Cell Anemia. Pollock and Dameshek (*Am. J. M. Sc.* **188**: 822, 1934) in describing elongation of the red blood cells in a Jewish family, review the often confusing terms which have arisen about this curious disorder. "Ovalocytosis" is said to be present when 10 per cent or more of the red cells are oval in shape. Elongation is the next degree of abnormality. When sickled red cells are present without anemia "sicklemia" is said to be present. An anemia in which sickled cells predominate is called "sickle cell anemia". Oval shaped and elongated red blood cells have now been frequently reported in members of the white race, although sickle-cell anemia has so far been described only in the colored. Pollock and Dameshek state that "it is probable that oval, elongated, and sickled red cells, and sickle-cell anemia represent various gradations in the same general abnormality of red blood cells". The disorder is fundamentally an hereditary one, and probably of no significance unless severe anemia is present. Diggs, Ahmann and Bibb (*Ann. Int. Med.* **7**: 769, 1933-34) demonstrated that a tendency of the red cells to sickle was observed in 8.3 per cent of 2539 Negroes when sealed moist preparations of blood were examined. These authors found that the ratio of sickle-cell anemia to the sickle-cell trait is about one to forty and that the trait itself has no significance. Corrigan and Schiller (*New Eng. J. Med.* **210**: 410, 1934) noted the presence in their autopsied cases of sickle-cell anemia, the ineffectiveness of liver, liver extract both by mouth and parenterally, desiccated hog's stomach, bone-marrow extract, iron, and transfusions.

"SPLENIC ANEMIA", BANTI'S DISEASE, ETC.

In most cases of continued enlargement of the spleen, leukopenia is a prominent feature and there is usually a distinct anemia together with some reduction in the blood platelets. Larrabee (*Am. J. M. Sc.* **188**: 745, 1934) suggested the term "chronic congestive splenomegaly" for this group of cases and pointed out their similarities despite the wide difference in etiological agents. Cirrhosis of the liver, syphilitic splenohematomegaly, chronic malaria, residual splenomegaly following various infections all may produce the same clinical state which, by the uncritical, is often called "splenic anemia" or Banti's disease. Whether there is such an entity as Banti's disease is open to question. (Most cases of alleged Banti's disease have in the reviewer's experience been finally diagnosed as chronic myelosis.) Increase in the pressure in any part of the portal circuit may result in splenomegaly, gastrointestinal hemorrhages, etc. The mechanisms of the leukopenia and slight anemia have not been worked out, although Larrabee suggested a possible diminution in "active principle" because of involvement of the liver.

Splenectomy will reduce the pressure in the portal circulation and thus reduce the dangers of hematemesis and ascites. Storti (*Haematologica* **15**: 107, 1934) and other Italian workers have recently advocated the use of ligation of the splenic artery as a simple and easier technique than splenectomy.

POLYCYTHEMIA

Etiology. Two main types are recognized: the idiopathic (polycythemia vera) and the secondary. The mechanisms involved in the secondary type are well brought out in a case reported by Waring and Yegge (*Ann. Int. Med.* **7**: 190, 1933). This patient had long-standing bronchial asthma and emphysema which undoubtedly produced anoxemia and cyanosis and was followed by polycythemia. The patient was working at a high altitude and this factor alone was sufficient to cause some degree of polycythemia. Possibly the pulmonary artery might have become sclerosed as the result of increase in the pressure within the lesser circuit. All of these factors tended to cause a greatly increased burden upon the heart. These authors discuss "Ayerza's disease", the conception of which has greatly changed since Ayerza described his "black cardiacs" in 1901. Castex, Capdehourat, and Repetto (*Arch. méd. chir. de l'app. respir.* **8**: 385, 1933) discuss the mechanisms in the development of this disease entity of chronic severe cyanosis and polycythemia. Although they do not minimize the importance of pulmonary artery arteriosclerosis as a factor, they stress the more fundamental factor of various types of chronic bronchopulmonary disorders which produce cyanosis. The individual affected, if his marrow is normal, reacts with polycythemia, a compensatory mechanism. Arteriosclerosis of the pulmonary artery, they feel, is secondary to the chronic bronchopulmonary disease. Heart disease need not necessarily be present. These authors feel that the reason the syndrome is not seen more frequently is that many older individuals with bronchopulmonary disease do not have a sufficiently reactive marrow.

The cause or causes of the so-called true polycythemia have not yet been discovered. Morris (*J. A. M. A.* **101**: 200, 1933) came out with an attractively simple hypothesis that the erythremia might be the result of hypersecretion of "addisin" (the so-called gastric hormone) or of hypersusceptibility of the marrow to it. He attempted to contrast pernicious anemia (due to a deficiency in "addisin") with polycythemia ("hyperaddisinism"). Unfortunately, these hypotheses have not stood the test of even a single year of investigation (cf.

also under Etiology of Anemia). Reznikoff, Foot, Bethea, and DuBois (*Tr. Amer. Physicians* **49**: 273, 1934) demonstrated that the blood-vessels of the marrow in cases of the idiopathic type of polycythemia showed unusual changes of the intima and media. These circulatory changes might be the initial factor which caused a great increase in the anoxemia of the marrow with resultant polycythemia. This author also pointed out that the disease was much more common among the Jewish population of New York City than in other groups and suggested an hereditary factor. Spodara and Forkner (*Arch. Int. Med.* **52**: 593, 1933) brought out the hereditary factor in their study of a large family of polycythemic individuals. The reviewer discovered this family trait in the affected family when one of the authors of the above paper was a medical student making classroom red blood cell counts. Boyd (*Am. J. M. Sc.* **187**: 589, 1934) describes a case characterized by polycythemia, duodenal ulcer, coronary thrombosis, and ascites and discusses the possibility that the ulcer might have had some bearing on the production of polycythemia; he feels, however, that the polycythemia was probably instrumental in causing the duodenal ulceration. Baserga (*Policlinico* **41**: 17, 1934) pointed out that polycythemia is occasionally associated with primary disease of the central nervous system particularly in the diencepho-hypophyseal region (acromegaly, encephalitis lethargica) and reported a case in which polycythemia was present in a case of pituitary neoplasm. It is possible that a red cell regulating mechanism is situated in the hypothalamic-pituitary portion of the brain.

Diagnosis. Most cases of polycythemia vera probably go unrecognized and are diagnosed as heart disease, angina pectoris, cerebral disease, peripheral vascular disease, etc. The reviewer has had occasion many times to comment on this fact. The infrequency with which routine erythrocyte counts are done and the inaccuracy of the Tallqvist hemoglobin test account to great extent for this state of affairs, which cannot be corrected unless one thinks of the possibility that the disease might be present and does a red cell count. One should consider the possibility in a patient with a dusky cyanotic appearance presenting vague symptoms which are frequently cerebral in type, at times circulatory. Sloan (*Arch. Neurol. & Psychiat.* **30**: 154, 1933) states that the disease has predominantly a nervous and mental symptomatology. This may be easily understood since the blood volume is increased, the cerebral vessels distended, the circulation slowed, and the viscosity of the blood increased. Schiff and Simon (*Ann. méd. psychol.* **91**: 616, 1933) describe a case characterized by cataplexia, chorea, and mental confusion. Bieling (*Med. Klin.* **29**: 1410, 1933) describes a severe case of Ménières syndrome due to polycythemia.

It is important for the practicing physician to be on the lookout for these cases, because much may be done with appropriate treatment.

Treatment. There has been no improvement in the fundamental treatment of polycythemia. Falconer (*Ann. Int. Med.* **7**: 172, 1933-34) suggests the use of venesection as an adjuvant to the use of phenylhydrazine hydrochloride. The reviewer has repeatedly used this method and finds it of value. If the erythrocyte count is eight to ten million per cu. mm., it is probably best to begin by removing from 500 to 1,000 cc. of blood and to begin phenylhydrazine therapy only when the red cell count is about 6.5 million. This procedure avoids excessive hemolysis and possible thrombotic complications which might ensue if large doses of phenylhydrazine were given immediately. Phenylhydrazine hydrochloride may be given either in capsules of 0.030 Gm. (½ grain) or dissolved in aqueous solution (1 dram — ½ grain). The original dosage is usually 0.090 to .150 Gm. daily, which is diminished to a maintenance dose of about 0.030 Gm. daily depending upon the individual patient. It is difficult to gauge the exact dosage, which must be individually adjusted. Vaquez and Mouquin (*Presse méd.* **42**: 1065, 1934) discuss the treatment of the disease with phenylhydrazine. They begin with a dosage of 0.050 to .100 Gm. and suspend medication in any event when the patient has taken a total of three Gm. They discuss the possible complications such as thrombosis and the rare examples of permanent cure. Falconer (*J. A. M. A.* **101**: 1633, 1933) report a case in which a remission has been present for eleven years following treatment with phenylhydrazine. Stone, Harris, and Bodansky (*J. A. M. A.* **101**: 495, 1933) are convinced that acetylphenylhydrazine is less toxic and provides a greater margin of safety in cases of overdosage; in two cases these authors were able to maintain a normal red cell count with only 100 mgs. weekly. The status of the various methods of treatment, including that by x-ray treatment over the bones, is discussed in a review of the subject in the *American Journal of the Medical Sciences* (**187**: 716, 1934). Phenylhydrazine easily holds first rank.

LEUKOSIS (LEUKEMIA)

Classification. There are three types of white blood cells: (1) the granulocytes, (2) the lymphocytes, and (3) the monocytes. These owe their presence in the blood stream to three separate sources: (1) the bone-marrow, (2) the lymphoid tissue, and (3) the reticulo-endothelial system. Leukemia might be better termed "leukosis" since it represents pathologically a generalized proliferation of the various types of white blood cells. Since three types of white blood cells and three separate blood-forming organs are present, three types of leukosis are possible: myelosis, lymphadenosis, and reticulosis.

The existence of monocytic leukemia, a third type of leukosis originating in the reticulo-endothelial system, has been abundantly confirmed. V. Levine (*Folia. Haemat.* **52**: 305, 1934) who reports nine cases, found that the disease was relatively common. The disease is called reticulo-endotheliosis by several authors. Gittins (*Arch. Dis. Childhood* **8**: 367, 1933) gives an excellent review of the subject together with a classification of the various types of reticulo-endothelial proliferations. He groups them as (A) Reactive (to blood destruction, sepsis, chemical abnormalities, (B) Focal Neoplastic (Reticuloma, etc.), and (C) Leucotic (Reticulo-endothelial leukosis or monocytic leukemia, leukemic and aleukemic). Foord, Parsons, and Butt (*J. A. M. A.* **101**: 1859, 1933) who report four cases of "leukemic reticulo-endotheliosis" also follow much the same type of classification. Callender (*Am. J. Path.* **10**: 443, 1934) in his review of the classification of the various types of leukocytic proliferation uses the term "Reticulocytoma, Leukemic". Most of these classifications, particularly those relating to reticulo-endothelial proliferations, are similar to those which have been published in European articles. The most comprehensive of these is that of Baserga.

The leukoses may be considered to be generalized proliferations of one of the white cell forming tissues. This proliferation may be associated with large numbers of circulating leukocytes or even with great diminution in their number. "Aleukemic leukemia", being a paradoxical term, is best replaced by using the terms aleukemic myelosis, lymphadenosis, and reticulosis. The fundamental pathological process is identical in both the aleukemic and the leukemic forms.

Etiology. The great majority of observers have finally agreed, after years of bickering, that the leukoses represent generalized neoplastic proliferations of one of the white blood cell forming tissues. This concept has recently received confirmation in the experimental laboratory at the hands of Furth, Seibold, and Rathbone (*Am. J. Cancer* **19**: 521, 1933) and of Büngeler (Editorial *J. A. M. A.* **102**: 1086, 1934). Both of these groups of investigators were able to induce leukosis in mice. The leukemic and sarcomatous lesions were frequently present together in the same mouse and transitions between one and the other state could often be seen. These lesions, leukemic or sarcomatous, corresponded chemically and biologically to those of malignant tumors. Furth (*J. Exper. Med.* **58**: 253, 1934) was also able to induce leukosis in chickens by means of injection of material free from viable cells. The "acute" leukoses, although resembling so closely severe infectious processes, should be regarded as highly malignant lesions composed of exceedingly primitive mesenchymal cells.

Diagnosis. Among the most frequently misdiagnosed conditions in hematologic practice are the aleukemic leukoses. Balbridge and Fowler (*Arch. Int. Med.* **52**: 852, 1933) state that five per cent of their cases of diffuse myelosis were permanently aleukemic. Their statement that "most physicians seem to regard aleukemic myelosis as an obscure form of hematopoietic disease which can be diagnosed only at necropsy" is heartily endorsed by the reviewer.

The acute leukoses when aleukemic are peculiarly enough to be differentiated from agranulocytosis. Many cases of so-called agranulocytosis are in all probability examples of acute leukosis. This view was stated by Dameshek (*J. A. M. A.* **102**: 950, 1934) who cited some of the diagnostic features, chief among which was the progressive anemia and reduction in platelets present in the leukotic process. Jackson (*Am. J. M. Sc.* **188**: 604, 1934) also cites these features and makes this epigrammatic statement: "Leukemia is still leukemia whether the white count be 50 or 50,000 per cu. mm." He stresses the value of the bone-marrow biopsy. Strumia (*Am. J. M. Sc.* **187**: 826, 1934) points out the transitions which may develop from extreme leukopenia to extreme leukemia in cases of leukosis. He goes too far, it appears, in attempting to link up the two conditions as being pathogenetically similar. The elevation in basal metabolic rate which frequently occurs in the chronic types of leukosis may be so striking at times as to suggest the possibility of hyperthyroidism. Dameshek, Berlin, and Blumgart (*New Eng. J. Med.* **210**: 723, 1934) comment upon this possibility and its possible implications. (See under Treatment.)

The diagnosis of the type of leukemia is relatively simple in the chronic varieties of the disease, but becomes difficult in the fulminating acute varieties when a primitive type of blood cell formation is taking place and extremely young cells are present in the circulation. Forkner (*Arch. Int. Med.* **53**: 1, 1934) takes up the diagnostic points by which the primitive cells (myeloblasts, lymphoblasts, monoblasts) may be diagnosed in a given case. In common with other authors, he states that the supravital technic is of particular value in the differentiation of the monocytic strain of cells, although in certain cases it is only by a combination of all the available methods of study (including that of oxidase staining) that an acceptable opinion concerning the cell type may be established. It is his opinion that the clinical picture of diffuse marked swelling of the mucous membranes, particularly of the gingivae usually associated with ulceration and necrosis is characteristic of acute monocytic leukemia

and usually absent in the other types. To this opinion the reviewer can only partially subscribe since the lymphatic type frequently gives very striking gingival and buccal lesions.

The heterophile antibody test, introduced in the diagnosis of benign lymphadenosis ("infectious mononucleosis") q.v., has been utilized by Bernstein (*J. Clin. Investigation* 13: 677, 1934) in the diagnosis of leukemia. This author found that heterophile agglutinins in the blood sera of twenty-one patients with leukemia were confined to low titers (less than 1 to 4) in twenty instances; whereas in most of the conditions simulating leukemia, heterophile agglutinins were found over a wider distribution of titer, up to one to sixteen. Bernstein brings out that the mechanism whereby antibodies are formed is disturbed in leukemia.

Treatment. The treatment of the leukoses continues to be unsatisfactory, although a patient with the chronic form may frequently be tided along for a number of years. Craver (*M. Clin. North America* 18: 703, 1934) gives in detail the plan of treatment for chronic myelosis in use at the Memorial Hospital, New York. Equal daily doses of x-rays are given over the spleen to total a mild erythema dose (about 600 roentgens). The cycle of treatment is finished in about a week and no further treatment for from three months to a year is necessary. The bones are also irradiated, the proximal ends of the long bones, the spine and the sternum being selected. Craver also cites his experience with arsenic (Fowler's solution) and believes it to be of value between cycles of x-ray treatment. (It is also of value when proper x-ray treatment is not readily obtainable.) He uses more guarded doses than those suggested by Forkner in 1930 and begins with three minims three times daily, raising the dosage by one minim per dose daily until the patient is taking about ten minims three times daily. (When x-rays are not being used, this dosage may be inadequate. It should be controlled by frequent leukocyte counts.) Portmann (*J. A. M. A.* 102: 178, 1934) states that chronic myelosis is ultimately a generalized disease, and that certain organs are affected in greater degree than others. Treatment by x-rays should therefore be individualized and should always be administered to the vertebrae, the ribs, and the sternum, at times the long bones. In the treatment of chronic lymphadenosis (lymphatic leukemia) Craver discusses very carefully the procedure of treatment by x-ray, depending in great part upon the regions involved, the leukocyte count, the patient's condition, and the metabolic rate. Cycles of treatment are given over the affected lymph-nodes and possibly over the mediastinal and retroperitoneal areas, if the patient's condition permits.

Because of the extreme elevation in basal metabolic rate which is so striking a manifestation of certain cases of chronic leukosis, particularly of the lymphoid type, Dameshek, Berlin, and Blumgart (*New Eng. J. Med.* 210: 723, 1934) conceived the idea that thyroidectomy might be of benefit. These authors point out that many of the symptoms of the disease (increased sweating, tachycardia, reaction to cold, etc.) may be part of the hypermetabolism rather than due directly to the leukotic process. In one case of aleukemic lymphadenosis with a metabolic rate of +65 per cent, there was striking relief of all the symptoms followed by complete regression of all the lymph-nodes and the spleen. The blood-picture became normal. This remission has persisted for one and a half years. These authors state that the procedure is worthy of further trial in similar cases.

There has been no advance in the treatment of the acute leukoses.

TUMORS OF WHITE BLOOD CELLS

Classification. Callender (*Am. J. Path.* 10: 443, 1934), the Registrar of the American Registry of Pathology, gives the following "semi-official" classification of tumors of the white blood cells: lymphosarcoma, myelosarcoma, and reticulum cell sarcoma. These may be leukemic and aleukemic. Hodgkin's disease is grouped among the reticulum cell proliferations. The reviewer has used much the same classification although he has subdivided the neoplasms a little further, chiefly according to the degree of cellular maturity. Thus, the generic terms for tumors of the lymphoid, myeloid, and reticulum cells (histiocytes) are myeloblastoma, lymphoblastoma, and histiocytoma. Lymphoblastoma is subdivided into lymphosarcoma (highly malignant) and lymphoma (relatively benign). Myeloblastoma (commonly called chloroma) is subdivided into myelosarcoma and myeloma. ("Multiple myeloma" is a lymphoid tumor composed of plasma cells and should be called plasmoma.) Histiocytoma is subdivided into reticulum cell sarcoma and reticulo(endothelio)ma. Any of these forms, particularly of the more malignant types may, by metastasizing into the blood stream, produce the picture of leukosis.

Diagnosis. The differential diagnosis of enlarged lymph-nodes is frequently very difficult. Held and Goldbloom (*M. Clin. North America* 18: 633, 1934) discuss a few of the differentiating points, but the reviewer has often found it difficult to distinguish between a pyogenic, tuberculous, carcinomatous, and lymphosarcomatous process by inspection and palpation. The diagnostic procedures which should be done in a given case are, besides physical examination, leukocyte counts, differential count of the white cells, tuberculin test, x-ray of the chest, possibly basal metabolic rate determination. In a

questionable instance, and even when the diagnosis appears obvious it is imperative to perform a biopsy of one of the affected nodes. This procedure is of more value than all the possible physical examinations and laboratory tests one may do.

Treatment. Craver (*M. Clin. North America* **18**: 703, 1934) reviews very carefully and very sanely the therapy of the malignant tumors of the white cells. He states that the fundamental plan of treatment is determined by asking the question as to whether the disease is localized and therefore offers some hope of cure, or whether it has spread so far beyond its source that treatment must be only palliative. Leucutia (*Am. J. M. Sc.* **188**: 612, 1934) says that radiation therapy must be considered the method *par excellence* in the treatment of lymphosarcoma. Thorough radiation therapy increases the expectation of life in all forms of lymphosarcoma from two and one-half to three and one-half years and leads to cure in at least ten per cent to fifteen per cent of the cases. (This is not the reviewer's experience; he is much more pessimistic.) Leucutia believes that it is essential to radiate the entire lymphatic system, regardless of whether the disease is localized or generalized. This causes "depletion of the blood" and requires careful management. He states that this drastic procedure leads at times to complete eradication of the disease, the outlook for the individual patient varying with the primitiveness of the cell, and the extent of involvement at the time of treatment. Anemia, cachexia, and fever usually render prognosis unfavorable.

HODGKIN'S DISEASE

The tendency in recent years has been to group Hodgkin's disease among the proliferative lesions arising from the reticulo-endothelial (monocytic) cells. Callender (ibid.) follows this grouping and it has been used by the reviewer (*Folia. Haemat.* **49**: 64, 1933). The disorder may be localized or generalized. If generalized, involving the lymph-nodes, spleen, liver and bone marrow, it may be said to be leukotic, and the reviewer described a case of this sort as "aleukemic reticulosis" (*Folia. Haemat.* loc. cit.). The most comprehensive review of the disease which has appeared in recent years is that of Wallhauser (*Arch. Path.* **16**: 522 and 672, 1933). This author takes up in great detail the many investigations which have been made in the attempt to show that the disease is of infectious (particularly tuberculous) origin. He does not appear to be enthusiastic about this possibility, and this feeling is shared by most investigators: namely, that Hodgkin's disease is not of infectious origin, but definitely neoplastic in type. Diagnosis cannot be made by the blood picture, which varies tremendously according to the stage and type of the disease. It is true that the blood picture shows more or less characteristic changes (providing one knows the diagnosis beforehand). Biopsy must be resorted to, and its importance cannot be overemphasized. Ogilvie and van Rooyen (*J. A. M. A.* **102**: 1842, 1934) report on the Gordon test which consists in injecting into the brains of rabbits some of the lymphoid material suspended in saline (after it has remained in the ice box for about a week). If the test is positive for Hodgkin's disease, the rabbits develop severe ataxia, incoördination, paralysis of the hind legs, and death. These authors found the test of value in two clinical cases. It needs further trial before its exact value can be demonstrated. The treatment of Hodgkin's disease is by persistent x-ray therapy, and this is commented upon by Craver, Leucutia and Wallhauser (all cited above). Leucutia (*Am. J. M. Sc.* **188**: 612, 1934) states that radiation therapy increases the expectancy of life, and produces five and ten year survivals in about one-third of the cases. This author uses very drastic treatment covering the entire lymphoid system.

BENIGN INFECTIOUS LYMPHADENOSIS (INFECTIOUS MONONUCLEOSIS, GLANDULAR FEVER)

Nomenclature. The term "infectious mononucleosis", suggested in 1922 by Sprunt and Evans and Longcope, is an unfortunate one since the cells concerned are not monocytes but lymphocytes; again how can a mononucleosis be infectious? Pfeiffer in 1885 described a group of cases in children which he called glandular fever, and this seems by far the better term since it is non-committal and clinically descriptive. Benign infectious lymphadenosis, although rather unwieldy, describes accurately the pathological process which is that of intense proliferation of lymphoid cells, a proliferation, however, which is benign (i.e., not leukemic or sarcomatous) and infectious in origin.

Etiology. The infectious nature of the disease is well known. Penati (*Minerva Med.* **25**: 414, 1934) in his comprehensive article, analyzes the various experiments which have been performed in an attempt to determine a specific etiological agent. The most promising results, he states, are those of Aage Nyfeldt who isolated a bacterium from the blood stream identical morphologically and culturally with that isolated by Murray, Webb and Swann from a highly contagious disease of rabbits associated with monocytosis. Nyfeldt called this organism *Bacterium monocytogenes hominis*.

Many authors have commented upon the frequency of the disorder in medical students, nurses, physicians, and members of physicians' families. Schulz (*München. med. Wchnschr.* **80**: 1809, 1933) had the unusual opportunity of observing an epidemic of the disease and was thus able to draw some inference regarding the incubation period, which he concluded was one week or less.

Pathology. The pathology of the disease has been but little studied since it is so benign a disorder and complications are so few. Penati (loc. cit.) describes the intense lymphoblastic hyperplasia which is exceedingly difficult to differentiate from the lymphoblastic proliferation of lymphosarcoma or of malignant lymphadenosis (leukemia).

Symptoms. Schultz (loc. cit.) was able to study thirty-five cases in an epidemic of the disease. Great fatigue and moodiness, particularly in children, usher in the disease and are soon followed by conjunctivitis, at times epistaxis, at times vomiting. Headache develops and becomes quite severe at times. The lymph nodes become enlarged and are the characteristic feature of the disorder. Schultz states they are frequently overlooked by the physician, and to this the reviewer emphatically subscribes. The nodes are frequently tender. The spleen is usually enlarged.

Blood Picture. All recent observers are agreed that the blood picture is that of a well-marked lymphocytosis with the presence of all types of abnormal lymphocytes. Stuart, Burgess, Lawson, and Wellman (*Arch. Int. Med.* **54**: 199, 1934) describe carefully the cytologic changes and state that all gradations in type between the small normal lymphocyte and the lymphoblast are seen. Most striking features are the vacuolated cytoplasm, often with irregular projections from the surface of the cell; the nucleus is frequently indented. The presence of all types of immature lymphocytes is properly stressed by these authors who were also able to observe amitotic division of the lymphocytes in the peripheral blood. Penati (loc. cit.) describes the lymphocytes and their many types very carefully; in other papers this author together with Levi (*Haematologica* **16**: 261, 1935) describes the lymphocytes and monocytes in the experimental infectious lymphadenosis of rabbits. It is the reviewer's opinion that the large lymphocytes of glandular fever may easily be differentiated from monocytes if the various characteristics of cytoplasm, granules in the cytoplasm, types of nucleus, character of nuclear chromatin, etc., are all kept in mind. The large lymphocyte has a sky-blue, pale-blue, or deep blue cytoplasm which is clear with only a few large granules, if any; the nucleus is only about one-half the size of the cell, round usually, and is made up of heavy chromatin blocks. The monocyte is gray-blue in color with many fine granules in the cytoplasm; the nucleus is large in comparison to the size of the cell, usually indented, and composed of a fine chromatin mesh. Further differentiation may be made from supravital studies (q.v.).

Diagnosis. Most of the cases, being mild, escape recognition through failure of the attending physician to palpate carefully for enlarged lymph nodes. The recognition of the disease among physicians and their associates is possibly due to the fact that a blood smear is frequently made. The blood picture is the most important diagnostic feature. The extreme lymphocytosis with so many immature lymphocytes suggests acute lymphatic leukemia, but this is ruled out by the course, the absence of anemia and reduction in blood platelets. Recently a new and interesting diagnostic test has been introduced. Described originally by Paul and Bunnell in 1932, the heterophile agglutination test has received abundant confirmation. Bernstein (*J. Clin. Investigation* **13**: 419, 1934) describes the technique and points out the diagnostic importance of agglutination of sheep's cells by the patient's serum in high titers. The details of the technique from an immunologist's standpoint have been investigated by Stuart in a paper by Stuart, Burgess, Lawson, and Wellman (*Arch. Int. Med.* **54**: 199, 1934). Stuart states that the presence of agglutinins for sheep erythrocytes in human blood was until recently of only academic interest. In glandular fever, these agglutinins become greatly increased so that positive agglutination may occur in as high a dilution as one to 5120.

A suspension of sheep's cells is added to successive dilutions of the patient's blood serum and after incubation for a few hours or after standing in the ice box overnight, the results are read. Stuart states that "with substantiating clinical and cytologic pictures, serums agglutinating in dilutions of 1-320 or more may well be considered positive". Van Ravenswaay (*New Eng. J. Med.* **211**: 1001, 1934) considers the test positive when complete agglutination occurs at a dilution of 1:32, but other authors (Bunnell, Bernstein) consider even 1:8 and 1:16 as positive results. Rosenthal and Wenkebach (*Klin. Wchnschr.* **12**: 499, 1933) state that those cases showing the clinical and hematological features of "infectious mononucleosis" but with a negative agglutination test are examples of "glandular fever" and to be differentiated from true "infectious mononucleosis". To this view the reviewer does not subscribe; possibly the agglutination test does not always give the correct information. It must be remembered, as van Ravenswaay points out, that the test is non-specific like the Weil-Felix test in typhus fever, which too may frequently be negative despite the typical features of the disease being present. It is comforting in a case which suggests acute lymphatic leukemia to obtain a positive agglutination test in high titer. Bernstein (*J. Clin. Investigation* **13**: 677, 1934) points out that in leukemia the titers are exceedingly low. The cause for the increased tendency on the part of the blood serum in the disease to agglutinate sheep's red cells has not as yet been worked out.

AGRANULOCYTOSIS (GRANULOCYTOPENIA, GRANULOPENIA, MALIGNANT NEUTROPENIA)

Etiology. Much speculation has taken place regarding the sudden prominence of agranulocytosis as a clinical entity. Until recently its etiology was a mystery. Kracke and Parker (*J. Lab. & Clin. Med.* 19: 799, 1934) list the following agents which had been at one time or another suspected: live bacteria, dead bacteria, hormonal products, radiation, and chemicals. None of these agents had been consistently implicated. Almost simultaneously, however, a group of articles appeared in which the etiology of the disease could be quite clearly traced to the use of a drug or drugs. Watkins in a short note (*Proc. Staff Meet. Mayo Clin.* 8: 713, 1933) implicated the barbiturates. Madison and Squier (*J. A. M. A.* 102: 755, 1934) were able to show quite conclusively in fourteen cases that amidopyrine and drugs containing amidopyrine had been used prior to the attack of agranulocytosis in all of their cases; they were able to reproduce the disease in two instances by giving the drug experimentally. Hoffman, Butt, and Hickey (*J. A. M. A.* 102: 1213, 1934) in re-investigating their fourteen cases of agranulocytosis demonstrated that all of them but one had taken amidopyrine prior to development of the disease; one had taken dinitrophenol. Rawls (*Am. J. M. Sc.* 187: 837, 1934), Holten, Nielsen, and Transbol (*Ugesk. f. laeger* 96: 155, 1934), Benjamin and Biederman (*J. A. M. A.* 103: 161, 1934) and others reported clear-cut instances of the disease following the ingestion of amidopyrine. Aspirin and the barbiturates appeared to be of no etiological importance, although Dameshek and Gargill (*New Eng. J. Med.* 10: 440, 1934), Bohn (*J. A. M. A.* 103: 249, 1934) and Silver (*J. A. M. A.* 103: 1058, 1934) showed that dinitrophenol—the drug so widely heralded in the treatment of obesity—had almost certainly brought about the disease in their cases. Kracke and Parker (*J. Lab. & Clin. Med.* 19: 799, 1934) in analyzing chemically the various drugs which had been implicated (neo-arsphenamine, arsphenamine, acetanilid, phenacetine, and amidopyrine) showed that they were all distinguished by the presence of a benzene ring with an NH_2 (amino) linkage; they therefore called the offending chemicals the "benzamine drugs". These authors postulated that the oxidation products of these drugs affected the bone marrow causing the disease (*Am. J. Clin. Path.* 4: 453, 1934). The rapid onset of granulocytopenia following a small dose of amidopyrine suggested to Benjamin and Biederman (*J. A. M. A.* 103: 161, 1934) that a hypersensitivity to the drug was present. This is of course borne out by the small number of actual cases of the disease in contrast to the millions of administrations of amidopyrine and other drugs, as noted by Reznikoff in the Special Report of the Council on Pharmacy and Chemistry (*J. A. M. A.* 102: 2183, 1934). The exact mechanism of this possible hypersensitivity has not yet been worked out. It can be stated definitely at present that amidopyrine is a potentially dangerous drug and that a certain few patients are unusually sensitive to even small doses of the drugs. The unusually large number of sedatives containing amidopyrine in combination should make one exceedingly cautious in their use. Jackson (*Am. J. M. Sc.* 188: 482, 1934) points out that the evidence for the incrimination of the above drugs is not altogether conclusive and multiple factors may be present.

Pathology. There is as yet no unanimity of opinion regarding the essential bone marrow pathology of the disease despite the number of autopsies which have been performed. The most careful of recent studies have been made by Jaffé (*Arch. Path.* 16: 611, 1933) who agrees with Fitz-Hugh and Krumbhaar (1932) that the most probable condition which exists is that of "maturation arrest", i.e., a condition in which mature polymorphonuclear cells in the marrow are not formed, although large numbers of primitive cells (myeloblasts and myelocytes) are present. Strumia (*Am. J. M. Sc.* 187: 826, 1934) points out the same thing, although he appears to go too far in attempting to bring leukemia into the same essential disease pattern as agranulocytosis, the difference he says being "a release which occurs in acute leukemias but not in agranulocytosis".

Diagnosis. Many uncritical observers diagnose as agranulocytosis almost any condition in which severe leukopenia is present. Doan (*J. A. M. A.* 101: 2075, 1933) brings out that only twenty per cent of the cases referred to his clinic with leukopenia are instances of true agranulocytosis. Dameshek (*J. A. M. A. Correspondence* 102: 950, 1934) points out many cases of so-called agranulocytosis are in all probability examples of aleukemic leukosis. This has been voiced by Jackson (*Am. J. M. Sc.* 188: 604, 1934). The disease may be considered to be a "selective" one involving only the bone marrow leukocytes, the red cells and the platelets not being affected. In any case in which anemia is striking or the hemorrhagic tendency pronounced the likelihood that one is dealing with agranulocytosis is remote. Pronounced constitutional symptoms in the presence of slight mucous membrane or throat signs, together with severe leukopenia (the red cells and platelets being essentially normal), are enough to make one suspect the presence of agranulocytosis. In most cases the count is below 2,000 per cu. mm. (usually below 1,000 per cu. mm.) and the polymorphonuclear cells are conspicuous by their absence.

Treatment. Up to the present time, the following methods of treatment for the disease

have been advocated: nonspecific therapy, transfusion of blood, "stimulating" doses of x-ray, nucleic acid derivatives (pentose nucleotides, adenine sulphate), "leukocytic cream", and liver extract. Reznikoff (*J. Clin. Investigation* **12**: 45, 1933) obtained good results with the use of adenine sulphate in eleven of fifteen cases. The drug is obtained from the Eastman Kodak Company in 5 Gm. lots. It is dissolved in 1 Gm. doses in 50 to 100 cc. of sterile salt solution with the use of heat (even boiling) and given slowly intravenously in daily or twice daily injections; reactions are rare. Dameshek (*New Eng. J. Med.* **209**: 1054, 1933 and *J. A. M. A.* **102**: 950, 1934) reports on its successful use without reactions in seven successive cases. Jackson's pentose nucleotides ("Pentnucleotide N.N.R.") have been used by many authors with good success. It is given in 10-20 cc. doses intramuscularly twice daily; 40 cc. may be given, and the intravenous route may be used. Dameshek (*New Eng. J. Med.* **209**: 1054, 1933) reports severe reactions with this drug and many authors are skeptical of the possible beneficial results. Reich and Reich (*Am. J. M. Sc.* **187**: 71, 1934) because they failed to produce bone marrow stimulation or increased maturation in rats with the drug concluded that the "results cast some doubt on the value of pentnucleotide in the treatment of agranulocytosis". It may be remarked that it is not always possible to carry over in toto to human beings results obtained from rats. Strumia (*Am. J. M. Sc.* **187**: 527, 1934) introduced "leukocytic cream" which represents the disintegration products of leukocytes obtained by centrifuging 150 cc. of whole citrated blood in cream separating bottles. The leukocytic "cream" thus obtained under aseptic precautions is injected intramuscularly daily in divided doses. Whether this method has any advantage over those of Reznikoff or Jackson remains to be seen. Brugsch and Lautsch (*München. med. Wchnschr.* **80**: 1014, 1933) and v. Bonsdorff (*Klin. Wchnschr.* **13**: 1079, 1934) have used liver extract intramuscularly with good results. It is thus seen that the nucleic acid derivatives and liver extract given parenterally are probably of value, although because of poor results obtained some observers doubt this. The question of tranfusion is a moot one; the reviewer has failed to note any benefit from its use. The outlook for recovery appears to vary with the observers. In the reviewer's own recent series of cases (unpublished) nine of twelve recovered. Early diagnosis and massive dosage with the above nucleic acid derivatives appear to be of greatest importance.

THE HEMORRHAGIC DISORDERS

Classification. Most observers are agreed that in the main there are two types of hemorrhagic disorders: purpura and hemophilia. Various types of purpura, however, are present, differing greatly in the essential mechanisms concerned. Some types of purpura are associated with a low blood platelet count (thrombocytopenic) and others with normal counts, the blood-vessel wall being presumably affected (non-thrombocytopenic).

Kugelmass (*J. A. M. A.* **102**: 204, 287, 1934) in a comprehensive paper on the hemorrhagic states in childhood proposes a classification based upon differentiating those cases presenting inherent defects in the blood-clotting mechanism itself and those in which the vascular endothelium is defective. He further subdivides the cases as follows:

A. Cases with defective blood-clotting mechanism
   1. Deficient prothrombin in new born→hemorrhagic disease of the new born
   2. Diminished platelets→thrombocytopenic purpura
   3. Deficiency of fibrinogen as in severe disease of the liver→increased clotting time
   4. Congenital defects of platelets, etc.→hereditary diseases such as hemophilia, thrombasthenia, etc.

B. Cases with defective vascular endothelium
   Malnutrition, scurvy
   Allergy
   Chronic infections—chemical poisons
   Hereditary defects of capillary structures

Farber (*Am. J. M. Sc.* **188**: 815, 1934) classifies the hereditary hemorrhagic disorders as follows:

Hemophilia—prolonged clotting time, platelet count normal.
Thrombopenic purpura—prolonged bleeding time, platelet count low.
Thrombasthenic purpura—prolonged bleeding time, platelet count normal.
Hereditary hemorrhagic telangiectasis (a vascular defect)—normal bleeding and clotting time, normal platelet count.

Farber was unable to put into this group a family of bleeders which he observed in which certain features in common with hemophilia, certain with purpura, were present.

The reviewer is inclined to agree with Kugelmass in dividing the hemorrhagic disorders into two main types: (1) those with an inherent defect of one of the blood-clotting factors, and (2) those in which the blood-clotting factors are normal but the vascular endothelium is defective. Clinically, however, two types of hemorrhagic manifestations are present: (1) the purpuric, and (2) the type distinguished by poor clotting of blood.

Etiology. Kugelmass (loc. cit.) lists the following etiological factors which may be present in a given case showing a hemorrhagic tendency: inadequate dietary (particularly in fats and vitamin C); use of various drugs; irradiation; in-

fections; diseases of the liver; diseases of the spleen; trauma and congestion; and diseases of the bone marrow. The hereditary factor is of course all-important.

In hemophilia the blood-platelets, although normal in number, are probably unable to form a normal clot; this defect is "genotypic", i.e., carried in the germ plasm. Purpura of the thrombocytopenic form is present in "destructive" conditions of the marrow (aplasia due to benzol, etc., tumor metastases, leukoses, etc.) and in the "selective" disorder of the marrow known as purpura hemorrhagica (Werlhof's disease) in which some defect in the bone marrow megakaryocytes is probably present. It is interesting in this connection to note that Lawrence and Knutti (*Am. J. M. Sc.* **188**: 37, 1934) found that a diminution in megakaryocytes was present in only two of six cases of purpura hemorrhagica in which bone marrow biopsy was done. On this account these authors felt that there are at least two different types of the condition in so far as the bone marrow is concerned and that the types in which megakaryocytes were present in the marrow would be more likely to profit by splenectomy.

The non-thrombocytopenic form of purpura is by far the most common type of hemorrhagic disorder encountered in practice, and in the reviewer's experience is frequently symptomatic of latent infection, a "toxic" process, senility, uremia, rheumatic fever, allergic processes, scurvy, etc.

Diagnostic Methods. Kugelmass (loc. cit.) lists the following procedures which are of diagnostic value: (1) A complete blood study (hemoglobin, red and white cell counts, examination of the stained smear). This rules out the presence of leukemic processes and various other hematologic abnormalities. (2) Determination of the clotting time, clot retraction, bleeding time, platelet count to indicate the type of change in the clotting mechanism which is involved. (3) In rare cases when the above factors are normal, the content of fibrinogen, prothrombin, and antithrombin. (4) Application of the tourniquet test (for capillary resistance); occasional use of the microscope for study of the nail bed (of value in hereditary hemorrhagic telangiectasis). Nygaard (*Proc. Staff Meet., Mayo Clin.* **9**: 492, 1934) has devised a test of the coagulability of the plasma which he finds is of value in the diagnosis of purpura hemorrhagica. In this condition, the coagulability of the plasma is greatly reduced, despite the fact that the coagulability of the whole blood is normal (test-tube method). Nygaard concludes that the test tube method cannot detect finer changes in the coagulability of the blood. Pemberton (*Am. J. Surg.* **24**: 793, 1934) points out the value of study of the morphology of the platelets from a stained smear by a competent hematologist. With this statement, the reviewer heartily agrees; one can frequently obtain as much information from the single examination of a well stained smear as from all the diagnostic procedures outlined above.

Because of a low platelet count and hemorrhagic manifestations, one should not immediately make the diagnosis of purpura hemorrhagica, but should remember that the same phenomena are present whenever megakaryocytes are destroyed (as in aplastic anemia, leukemia, etc.). Neither is every case presenting ecchymotic spots an example of purpura hemorrhagica; usually the reverse is true and platelets are abundant. Search should then be made for some underlying condition: infectious, toxic, etc.

Treatment. For hemophilia, no acceptable method of treatment has been found despite the enthusiasm which was engendered by Birch's reports in 1931 and 1932 of the striking therapeutic responses to ovarian extracts. Stetson, Forkner, Chew, and Rich (*J. A. M. A.* **102**: 1122, 1934) in a carefully conceived study, were able to demonstrate that theelol orally, soluble ovarian substance intramuscularly, ovarian substance orally, fresh whole beef ovary orally, aqueous extract of fresh whole beef ovary orally, solid residue of ovarian tissue orally, and theelin subcutaneously all were completely without effect on the coagulation time in seven cases of hemophilia. Several other authors have confirmed these results. Jones and Tocantins (*J. A. M. A.* **103**: 1671, 1934) review the entire field of hemophilia and conclude that transfusion of blood constitutes the best method for the prevention and treatment of acute attacks of bleeding. They also found that intramuscular injection of whole blood has seemed to benefit some patients and that fresh serum was a satisfactory local hemostatic agent.

In the treatment of purpura hemorrhagica, splenectomy still holds first place as the method most likely to bring about remission. Pemberton (*Am J. Surg.* **24**: 793, 1934) states the problem from the surgeon's standpoint. He says that the procedure is often life-saving, and that remissions permanent in degree are present in sixty-three per cent of the cases. The operative hazard in the chronic type is "minimal". He does agree, however, that in cases which are incipient or mild, splenectomy is rarely indicated. The reviewer would even go farther. It seems best to attempt all forms of palliative therapy in this disease which is so subject to remissions and relapses. We are now seeing more and more cases of recurrent bleeding following splenectomy. Among palliative methods to be used Kugelmass (loc. cit.) cites high protein and high fat diets, elimination of infectious foci, regulation of ovarian dysfunction by the use of the various pituitary and ovarian hor-

mones, injection of whole milk intramuscularly, transfusion of blood, etc. It is also wise, in the reviewer's experience, to use various vitamins in large concentration (A, B, C, D) and possibly to give liver extract and iron. When bleeding manifestations are numerous, it may be worth while to try some of the newer methods of therapy: the use of ascorbic acid (Merck) (vitamin C) given in solution intravenously as suggested by Böger and Schröder (*Munch. med. Wchnschr.* **81**: 1335, 1934). These authors found that the daily intravenous administration of 100 mgs. of ascorbic acid was effective in controlling capillary bleeding even though the blood platelets might be diminished. The capillary wall is an important factor even when the platelets are reduced. Landau and Hejman (*Presse méd.* **42**: 174, 1934) observed that there might be no correlation between the signs of bleeding and the platelet count and bleeding time and suggested that variations in the contractility of the blood vessels might occur. Vitamin C probably acts on the capillary endothelium and this may be the rationale for its action. Similar reasoning is behind the recent use of moccasin snake venom therapy in the hemorrhagic states, as suggested by Peck in 1932 (Peck and Goldberger, *Am. J. Obst. & Gynec.* **25**: 887, 1933). The venom (obtainable from the Lederle Co.) is used in dilutions of 1:3000 in physiological saline and injected subcutaneously in gradually increasing doses usually twice weekly and for a length of time depending upon the type of case concerned. Peck was able to control bleeding in purpura hemorrhagica even though the platelet count did not rise, again suggesting that the venom has a direct action in capillaries.

An antivenom preparation (antivenin) has been in use for several years in the control of the hemorrhagic states. Taylor (*Am. J. Surg.* **21**: 285, 1933) reports on several cases which have been treated in this fashion. (Antivenin may be obtained in 10 cc. vials from certain drug houses and is injected intramuscularly after a preliminary test for sensitivity.) Taylor states that the antivenin of certain South American snakes has greater efficacy than that obtained from the moccasin snake. The reviewer, in a limited experience, feels that it is worthy of further trial; in two cases bleeding stopped after injection of the antivenin. Whether this was coincidental is debatable. Savagnome (*Policlinico* **41**: 763, 1934) found that calcium gluconate given intravenously increased the platelet count somewhat, but his results are not at all conclusive. Jones and Rathmell (*Tr. A. Am. Physicians* **49**: 277, 1934) in a carefully controlled study found that large doses of viosterol had no real effect on the platelet count either in normal subjects or those in whom purpura was present.

With respect to transfusion, debate still continues regarding the relative merits of the direct versus the indirect methods. There can be no doubt, as Lundy (*Minnesota Med.* **17**: 699, 1934) states, that the indirect method with the use of sodium citrate is simply and readily performed and no more formidable than any intravenous procedure. Lundy suggests administering the blood slowly, about fifteen cc. per minute. When many transfusions are done, a direct method (the reviewer uses the Scannel) is preferable because the blood is unmodified, there is less handling, etc. From Soviet Russia has recently come an interesting suggestion: the use of stored blood obtained either from professional donors or even from cadavers shortly after death. Irger and collaborators (*Novy. Khir. Arkhiv.* **32**: 53, 1934) report on this method and on their studies with experimental conservation of dog's blood. They conclude that because of various morphologic and biologic alterations which occur, the value of conserved blood for purpose of transfusion is much less than that of fresh blood.

In the non-thrombocytopenic forms of purpura, a vigorous search should be conducted for latent infections, even lues. Calcium in large doses is frequently of value. The reviewer uses calcium gluconate 1.5 Gm. every three hours by mouth together with milk, and at times gives the same drug intramuscularly.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 21431

PRESENTATION OF CASE

A seventy year old Hebrew potato merchant entered complaining of cough productive of yellow material.

Four months prior to admission he had pneumonia involving the left lung. At this time there was a high leukocyte count and a negative blood culture. The sputum contained type IV pneumococcus. He convalesced slowly and one month after the onset of his acute illness suffered a relapse which confined him to bed for two weeks. Subsequently he recovered and returned to his business. He continued working for six weeks although he felt weak and markedly short-winded. His breathing became wheezing in character. A productive cough which had been present with varying intensity for thirty-three or more years continued with somewhat increased severity. About two weeks before admission, following undue exertion, he felt "grippy and feverish". The following day he was found by his physician to have paroxysms of auricular fibrillation. Râles were audible at both bases and at the right top anteriorly and posteriorly. There was no leukocytosis at this time. Following this his temperature began to rise to 103° or 104° each night. His sputum increased and became purulent but had no foul odor. He slept poorly and was often irrational at night. His leukocyte count rose to 37,000 two days before admission.

At the age of forty, thirty years before entry, he had been sent to Colorado because of cough and "germs" in his sputum. He remained there for five years but had a very active existence following his return East. At an examination eleven years before admission, when fifty-nine years of age, râles were found over the right apex. Five years later definite medium crepitant râles were heard at both bases, more on the left. In the following year a prostatectomy was performed. Three years before admission, following physical strain, he first coughed up blood. At this time medium crepitant râles were heard at the left base and axilla. There was no fever. No tubercle bacilli were found in his sputum.

Physical examination revealed a well-developed and nourished old man who was suffering from considerable respiratory distress. Except for slight pallor the skin and mucous membranes were normal. There was slight cyanosis of the nailbed and a suggestion of parrot beaking of the nails. The right pupil was slightly smaller than the left and both were contracted, presumably as a result of administered morphin. The teeth were in only fair condition. The tonsils were red and lumpy. The heart was not enlarged to percussion, nor were there any auscultatory abnormalities noted. The blood pressure was 110/60. The brachial vessels were soft. The lungs were examined with the patient lying on the left side. There was dullness on the right side extending with increased intensity from the second rib to the upper border of the liver dullness. Posteriorly there was only slight impairment of resonance of the right chest from the upper border of the scapula to the base. On the left side there was some hyperresonance. The breath sounds were generally diminished in intensity, except for an area inferior to the right clavicle where bronchial breath sounds were obtained. Constant sibilant râles were audible throughout both sides and there were coarse crackling inspiratory râles at the left bottom posteriorly. Vocal resonance was diminished in the area of dullness. A lipoma in the region of the left costovertebral angle precluded examination here. The abdomen was slightly distended and tympanitic. The liver and spleen were not palpable. Neurological examination was negative except for absent knee jerks.

The temperature was 102.5°, the pulse 100. The respirations were 24.

Examination of the urine revealed normal specific gravity and a slight trace of albumin. The sediment contained 3 to 100 white blood cells. The blood showed a red cell count of 4,700,000, with a hemoglobin of 65 per cent. The white cell count was 42,800, 83 per cent polymorphonuclears. Four sputum examinations revealed thick mucopurulent material which was negative for tubercle bacilli and elastic tissue. The stools were negative. The non-protein nitrogen of the blood was 20 milligrams per 100 cubic centimeters. A Hinton test was negative. The icteric index was 4. A blood culture exhibited no growth.

X-ray examination showed dullness in the region occupying the greater portion of the right upper lobe. The inferior margin of this dull area ended in a sharp horizontal line laterally. There was a lobulated shadow in its medial aspect which appeared to lie in the region of the lung root and was about two inches in diameter. The diaphragm, heart and mediastinum were normal.

On the day of admission an exploring needle introduced in the third right interspace in the midaxillary line elicited definite resistance which

increased after passing the pleura. A small amount of bloody fluid was withdrawn. On the fifth day a thick, creamy, odorless pus was removed from the third right interspace posteriorly. Microscopic examination of this exhibited pus cells and gram-positive organisms resembling pneumococci. X-ray at this time showed a small quantity of fluid in the posterior aspect of the right pleural cavity. On the following day under local anesthesia a resection of the third right rib was done. At the end of the second week the only significant change in the physical findings was a return of resonance at the right bottom anteriorly. Flatness was present in the infraclavicular region on this side. By the end of the third week the entire right side was dull. An x-ray film showed the small area of dullness in the right side of the chest to be increased. The operative wound was cleaned of granulation tissue and a half ounce of creamy pus was extruded. At this time the patient's chief discomfort was a constant hacking cough with inability to raise sputum. During the entire hospital stay the temperature remained between 100° and 104°, with an evening rise which averaged about two degrees. His pulse, despite the fact that he received 36 grains of digitalis within one week and a grain and a half daily thereafter, remained elevated, ranging between 100 and 160. The respirations varied, being from time to time between 30 and 60. The leukocyte count ranged from 26,000 to 37,000. During the fourth week the patient seemed to be improving. Shortly afterward, needle taps into the right second, fourth and seventh interspaces medial and lateral to the midclavicular line revealed resistance but no pus, air or blood. X-rays at this time showed an increase in the dullness of the right upper chest with some increase in the amount of fluid. The outline of the right side of the diaphragm was obliterated in its lateral half. The trachea was displaced toward the left in the region of the aortic arch. The right lower lobe contained only a small quantity of air. During the fifth week the patient developed considerable difficulty in coughing and his respiratory passages seemed filled with secretion. He died on the forty-eighth hospital day.

Differential Diagnosis

Dr. James H. Means: I do not know of any occupational hazard pertaining to potato merchandising so I think we must pass that over.

I think it is easiest to get a lucid and simple impression of this case by beginning with the past history rather than the present illness because I suspect that they are related.

We note above in the present illness that he had had a productive cough for thirty-three or more years. Indeed he had had a productive cough for about half of his life, and it is of interest that it began some few years before he was sent to Colorado. That is all we know about this illness forty years ago. If he was told that he had germs in his sputum he was undoubtedly told he had tubercle bacilli. I cannot conceive of a doctor telling him about any other germs or sending him to Colorado for any other reason; so he either had or was thought to have pulmonary tuberculosis at that time. He remained there for five years and apparently made a good recovery because he was able to lead an active existence after his return East.

"At an examination eleven years before admission . . . râles were heard at both bases, more on the right." I do not know where the examination was made. I should like to know what else was present at that time but that single finding is perhaps of interest. Our attention is directed toward the right apex. It certainly could have been a chronic tuberculous process which was lingering on. It may not have been active because one may have râles without actual tuberculous activity. One can also have a non-tuberculous infectious process in an old tuberculous cavity. This basal process, however, which is bilateral and was found some years later, interests me a good deal and when I am told that a man of seventy who has had a productive cough for half of his life has râles at both bases I am led to suspect that among other things he has some degree of chronic bronchiectasis, or something on that order.

In the following year a prostatectomy was performed. We do not know why. There is no mention of symptoms connected with that part of his body.

Three years before admission he coughed up blood. We do not know how much. He might have coughed it up because of an old tuberculous process, of course, or because he had bronchiectasis.

"At this time medium crepitant râles were heard at the left base and axilla." They had been heard at both bases prior to this.

"No tubercle bacilli were found in his sputum." Of course that does not mean he did not have tuberculosis before. Now going back to the first paragraph we are told that four months prior to admission he had pneumonia involving the left lung. We do not know anything about it, we are simply told he did have pneumonia. At this time he had a high leucocyte count and negative blood culture, and the sputum contained a type IV pneumococcus. I would feel that he either had pneumonia or something else. He convalesced slowly and one month later suffered a relapse which confined him to bed for two weeks. He subsequently recovered and returned to business, continuing work for six weeks although he felt weak and shortwinded. In other words, he did not recover completely.

I am interested in the wheeze probably as

pointing to something involving the bronchial tract.

This productive cough which he had apparently for thirty-three years became intensified at this time.

"The following day he was found by his physician to have paroxysms of auricular fibrillation." That is not really significant. Anyone of seventy may have paroxysms of auricular fibrillation, particularly when an infection has persisted. It might be present in a patient with arteriosclerotic change in the heart.

It seems to me we can draw certain inferences from the history. I think in all probability he did have tuberculosis and I think very likely he had in addition a chronic pulmonary disease, bronchiectasis which was not tuberculous. It is entirely possible for an individual to have both. The present condition suggests that he had a purulent process in the chest because he was developing a fever and running a high leucocyte count and was getting up some purulent sputum; so that the history points to his chest and to this lung and suggests that he has a chronic suppurative process of some kind, a suppurative process in the pleura communicating with the bronchus.

The fact that he is well developed and nourished on physical examination is of interest in a man suffering from a chronic disease. It shows good resistance to it. It had not caused any state of cachexia. Of course people with tuberculosis will go on for many years with lungs filled with cavities and remain fairly well and in a good state of nutrition. I have seen such cases, and I am sure we all have.

It appears that the heart is not the seat of his trouble.

"The lungs were examined with the patient lying on his left side." I do not know why they were examined in that position and it does not state whether they were examined in any other position. I do not know whether that was the only position he was able to assume or whether there was any special virtue in that position.

"There was dullness on the right side extending with increased intensity from the second rib to the upper border of the liver dullness." That area of dullness is more in the region of the middle lobe than of the other lobes. It makes us wonder if perhaps the seat of this difficulty is not in the middle lobe, either wholly or in part. The signs are chiefly in front which would fit with a middle lobe lesion. On the left side where he may have had pneumonia there was some hyperresonance.

"Constant sibilant râles were audible throughout both sides and there were coarse crackling inspiratory râles at the left bottom posteriorly." That would fit with our conception of an initial process in both bases of a bronchiectatic nature. I should like to know something more about the physical signs in the region of the right middle lobe. I do not see any mention of the tactile fremitus. I should interpret these signs at least as being consistent with a process in the lung field, one of consolidation and very likely in parts of it at least with plugging of the bronchus bringing about a diminution in the breath sounds.

I infer from the history that he had a suppurative condition in his lung, probably of a fairly recent origin, because I should be rather more inclined to explain the chronic symptoms on the basis of either an old tuberculous process of the right apex or this bronchiectasis, which I suspect he may have at both bases, and that the recent lesion is a suppurative one somewhere in the middle of his right chest. I think the physical findings are consistent with such an interpretation of the history and indicate that the lesion is in the anterior part of the right chest in the region of the middle lobe. I fancy that there must be a good deal of induration of the lung about the suppurative lesion and very likely some atelectasis.

The blood shows a moderate hypochromic type of anemia which anyone with chronic infection might have. He has a high leucocytosis which would go with a purulent condition and would suggest that the pus was not draining well, also with a high fever.

I went as far as I could with these x-rays and I was not certain that the lesion clearly was in the upper lobe. I still think it could be middle lobe. It is unwise to disagree with the radiologist and I do it only in a sporting sort of fashion. There are a lot of dense spots in the left side that could be miliary tuberculosis, I suppose, and down at the bases some thickening that I think might go with my theory of an old bronchiectasis. Then there is a lesion in the middle of the right chest which is very peculiar. It has a flat bottom, out here is a straight line which could be, I suppose, the margin of the middle lobe with perhaps some fluid encapsulated in the interlobar space, and a most remarkable lesion toward the hilus which is dense and seems to be nodular. There are several parts to it. In the next picture it appears as though a cavity had been emptied.

There are some other interesting features. I was impressed that the ribs were close together on the right. The right chest is smaller than the left.

To go on with the story—"On the day of admission an exploring needle introduced in the third right interspace in the midaxillary line elicited definite resistance which increased after passing the pleura." Apparently they plunged their needle into something solid. On the second attempt they struck a hole, apparently, and obtained thick, creamy odorless pus. The fact that it was odorless might indicate that it was not of very long duration.

There was fluid at times in the base and I suspect it had been released from the lung in the process of paracentesis and thus was found at the bottom of the pleural cavity.

Whatever happened, the fluid disappeared. Of course, it might be simply an accumulation of serous fluid of an irritative sort that was rapidly taken up. One sees it in the chest for example in connection with abscess of the liver. It could have been due to something like that.

Of course the pulse would not be slowed much by digitalis because its rapidity is due to toxemia.

I should say at this point that they had attempted to drain a cavity, indeed they had drained a cavity, but he still presented the picture of undrained pus from which I would infer that there was more than one cavity.

Those in charge evidently thought the same and tried to find other pus pockets but did not succeed.

"The trachea was displaced toward the left in the region of the aortic arch." I should like to ask the radiologist about that. I cannot understand why it should be displaced toward the left if the right chest is smaller and there is atelectasis.

To summarize and interpret the findings in this case then, I would say that here was a man who had had three episodes related to his lungs over a period of four months, the first of which he was told was pneumonia on the left side.

During his stay in the hospital he presented evidence of a suppurative process in the right lung, which I believe to have been multiple abscess with a good deal of induration and atelectasis. I also believe that he had empyema probably resulting from the spilling of pus during paracentesis.

I believe that he has old pulmonary tuberculosis, and an old bilateral bronchiectasis. I am puzzled about what relation these old processes bear to the more acute terminal one.

I raise the question of an old healed miliary tuberculosis.

I think of malignant disease of the lung with secondary suppuration, but I cannot feel that we have the evidence to assert its presence.

That is as far as I can go.

X-ray Interpretation

Dr. Aubrey O. Hampton: We had as much difficulty with this patient as Dr. Means has had, and in fact Dr. Lord and I had quite a discussion over him. He had this complete consolidation of the lower aspect of the upper lobe and, as Dr. Means says, it does extend down forward here to the diaphragm and the middle lobe might well have been involved. We could not see the top of the middle lobe, so we did not know for certain. The thing that interested us most was this round shadow here, and this irregular nodular shadow here at the lower aspect of the right lung root. The question was whether that was a tumor or not, whether that produced the whole picture; certainly it looks like a tumor. The complication is this which is probably bronchiectasis at the left base and perhaps bronchiectasis of the right middle lobe; or you could say that this was bronchiectasis and this was bronchiectasis; and all we have in addition is a consolidated right upper lobe.

Dr. Means: Is that a cavity with fluid level?

Dr. Hampton: We could not find a cavity that we were sure of. We took this Bucky film in an effort to show cavities. If this is tumor, why should not the heart shift toward the right? Apparently the trachea shifted in the opposite direction. We tried to explain that without much success. We did not find anything except calcified old tubercles in the left lung and these few dilated bronchi at the left base.

Clinical Discussion

Dr. Frederick T. Lord: Our conclusions were in accord with those of Dr. Means with respect to the probability of an old pulmonary tuberculosis and also of bronchiectasis at the left base. The complex of physical signs over the right upper part of the chest as presented in the case history is incomplete. Dr. Means was, in consequence, at a disadvantage in interpreting the significance of the signs. They varied somewhat from time to time. In the right upper front there was dullness, diminished breathing, voice, whisper and tactile fremitus. At times, bronchial breathing was heard over the inner upper part of the dull area. These findings, with the roentgenologic evidence of a dense mass in the region of the right root, suggested obstruction of the right upper lobe bronchus due to malignant disease. The clinical aspects and the x-ray also suggested the possibility of encapsulated pleural fluid in this region. The tapping on the fifth day was done in the third interspace in the right upper axillary region and between one and two cubic centimeters of pus containing pneumococci (later shown to be type VIII) were obtained at what seemed to be the level of the pleura. It was, in consequence, thought that he had an encapsulated empyema, but at operation by Dr. Churchill the pus was found to come from multiple small areas in the lung and not from the pleura. The finding of pneumonitis and cavity formation due to pneumococcus infection is of some interest because of its rarity. In explanation, it may be suggested that the usual factors leading to resolution of pneumococcus pneumonia could not operate under the pathologic conditions and that the absence of access of blood with its antienzyme permitted the unrestrained digestive action of enzyme on the lung framework.

Clinical Diagnoses

Carcinoma of the lung?
Bronchiectasis.
Old tuberculosis.
Empyema, right.
Bronchopneumonia.

Dr. James H. Means's Diagnoses

Multiple abscesses, right lung.
Pulmonary atelectasis, right.
Empyema, right.
Old tuberculosis, right top.
Chronic bronchiectasis, both bases.
Cancer of the lung with secondary suppuration?

Anatomic Diagnoses

Oat-cell carcinoma of the lung, right upper, with metastases to the regional glands.
Bronchopneumonia, right upper.
Empyema, encapsulated, right.
Compression atelectasis, right middle and lower.
Bronchiectasis, left lower.
Pulmonary tuberculosis, healed, left upper.
Pulmonary emphysema, left.
Pulmonary osteoarthropathy, slight.
Arteriosclerosis, slight, aortic.

Pathologic Discussion

Dr. Tracy B. Mallory: The autopsy findings are in part confirmatory and in part rather surprising. The most immediate finding on opening the thoracic cavity was that we broke into a very large empyema cavity on the right side which lay between the diaphragm and the base of the lung. It contained about a liter of pus and had thick walls. It was difficult to estimate how long it had been present but it certainly must have been there a couple of weeks. The lower lobe and middle lobe were completely atelectatic, probably from compression between the empyema cavity and the consolidated upper lobe. The bronchus to the right upper lobe was completely occluded by a mass of tumor which was infiltrating in rather fan-shaped fashion the entire lobe. The lung abscess found by Dr. Churchill had been adequately drained and had nearly healed. On the left side there was a localized area of bronchiectasis at the left base and the other lobes were essentially normal, with slight compensatory emphysema.

A Physician: Was there any tuberculosis at the right apex?

Dr. Mallory: The left apex had a small tuberculous scar. That was all the evidence of tuberculosis that we found. The right upper lobe beyond the obstruction of the bronchi was largely atelectatic, to a certain extent chronically infected. There were no obvious cavities at the time of autopsy.

A Physician: What was the tumor?

Dr. Mallory: It appears to be an oat-cell carcinoma, quite typical.

Dr. Edward D. Churchill: The empyema that was found at autopsy probably came in the last two weeks in this illness and at that time we had practically decided he had an advancing malignant disease because of the operative findings and the physical signs of bronchial obstruction.

CASE 21432

Presentation of Case

A fifty-seven year old white American widow was admitted to the surgical service complaining of increasing weakness and bleeding from the rectum and vagina.

She had been well until three years previously. At this time her menses, which had always recurred regularly at monthly intervals and lasted for three to four days, suddenly became irregular. The intervals varied from three to ten weeks and the duration extended to one week. The flow was quite profuse and contained many large clots. There was no associated distress. She considered this the result of her menopause and continued with her normal activity until one year prior to entry. At this time she began to lose her appetite, and her diet was gradually limited to fruits, soft foods and milk. She lost thirty pounds during the year before entry to the hospital and became progressively more readily fatigued so that she was compelled to discontinue her housework and spend most of the day in bed. About one month before admission she first noted fresh blood and clots in her stools associated occasionally with tenesmus and cramplike "gas pains". She had always been constipated and took a laxative each day. For three days before admission she had frequent desire to go to stool with the passage of blood and clots.

At the age of forty-eight she had complete amenorrhea for a period of ten months. Subsequently the previous cycle returned. She had typhoid fever at the age of fourteen.

Her mother died of gastric hemorrhage resulting from an ulcer at the age of forty-seven. Her father died of a stroke at the age of seventy-five.

Although married for twenty-five years the patient had no children. There was a questionable miscarriage after one month of amenorrhea.

Physical examination showed a well-developed, rather obese woman in no apparent distress. There was slight exophthalmos but the eyes were otherwise negative. The heart was enlarged to the left. There was a loud blowing systolic murmur audible over the precordium.

The blood pressure was 174/84. Palpation of the abdomen demonstrated a firm slightly tender rounded mass in the right lower quadrant, extending from within the pelvis halfway to the umbilicus. Vaginal examination showed that the mass was connected with the uterus. Rectal examination elicited a sphincter so spastic as to preclude demonstration of further details.

The temperature was 100°, the pulse 88. The respirations were 20.

Examination of the urine showed a slight trace of albumin with a specific gravity of 1.002 to 1.012. There was no sugar present. The sediment contained on one occasion many red blood cells but in other specimens there were few or none. It was, however, loaded with white blood cells and contained an occasional cast. The blood showed a red cell count of 2,030,000, with a hemoglobin of 40 per cent. The white cell count was 12,350, 81 per cent polymorphonuclears. The platelets were normal. The blood Hinton and Wassermann tests were strongly positive. The nonprotein nitrogen of the blood was 57 milligrams.

On the second day a proctoscopy was done. The proctoscope passed for a distance of eight and a half inches. The bowel was not dilatable beyond this point and a slot-like opening with considerable bleeding was observed. A biopsy was done. That night the patient's temperature suddenly rose to 103.8°. She became somewhat drowsy but talked coherently. On the next morning she was comatose, cyanotic, incontinent and had Cheyne-Stokes respiration. The pupils were constricted and fixed. There was a bilateral Babinski sign. The temperature remained elevated but the pulse dropped to 70. The blood pressure was 90/40. A lumbar puncture showed an initial pressure of 200 millimeters. The fluid was clear and negative. She improved gradually, became less comatose and on the fifth hospital day was transferred to the neurological service. Examination there demonstrated a definite exophthalmos. The pupils were constricted, equal and reacted to light and distance. The heart findings were unchanged. The blood pressure had risen to 156/54. There was dullness and diminished tactile fremitus at both lung bases posteriorly. Breath sounds were present and appeared to be coarsened. The bladder was found to be halfway to the umbilicus. The patient was fairly well oriented but remained semistuporous for the greater portion of the examination. The right knee jerk and ankle jerk were slightly greater than the left. The Babinski sign was absent. The remainder of the neurological examination was negative. Subsequently there was definite mental improvement. A portable x-ray of the chest on the eighth day showed a mottled area of dullness in the right upper lung field and another below the right hilus. Four days later the consolidation in the right upper lobe had decreased. There was no great change in the patient's general condition until the beginning of the third week. At this time echolalia, increasing distention of the abdomen, and enlargement of the tumor mass in the right lower quadrant were noted. A positive Babinski sign appeared on the left side. On the twenty-third hospital day the temperature rose rapidly to 105°, the pulse was 100 with many dropped beats, and the respirations became shallow with the rate of 50 per minute. There was dullness at both bases posteriorly with bubbling râles on the right. Her breathing became Cheyne-Stokes in character and the temperature rose to 107°. The patient became comatose and expired that day.

Differential Diagnosis

Dr. Arthur W. Allen: This is a rather complicated story of a woman who has lues and who comes in at the age of fifty-seven bleeding from the vagina and rectum. We have certain evidence that there is a tumor in the pelvis which probably is quite significant. The omission of any note as to whether this tumor was expansile I think in this instance, even in a luetic, is not important. With the story as presented, one thinks in this type of case of a carcinoma of the body of the uterus which has now become quite widespread and has involved the lower large bowel, so that you have not only bleeding from the vagina but bleeding from the rectum as well.

The important thing that is omitted from the history that we should like to know is the character of this discharge that she had from the vagina. It simply mentions blood and clots, nothing about the odor. In carcinoma of the fundus of the uterus you frequently get a very foul discharge which is quite characteristic.

In the sequence of events one wonders what happened in the proctoscopy to cause the temperature to rise so rapidly. Perhaps there was no connection between this examination and the definite increase in the patient's illness. Also, there was a biopsy taken which is withheld from us.

Dr. Tracy B. Mallory: We will be glad to tell you that, Dr. Allen. It showed adenocarcinoma.

Dr. Allen: That is extremely helpful because we now know that the patient not only had lues but adenocarcinoma as well. Of course the thing that interests us is whether this could be a primary bowel lesion. Could this uterine condition have been a fibroid or an ovarian cyst in the pelvis and the real lesion be in the bowel itself? I think we probably can feel pretty sure that the right sided mass does not mean primary carcinoma in the cecum. She comes in with enough anemia to fit such a diagnosis, but I would question whether she would go three

years with symptoms of this sort with a primary lesion in the cecum.

One wonders about the cerebral accident that happened in the hospital. Was it due to metastatic malignant disease, lues, hemorrhage or anemia of the brain. The spinal puncture would help somewhat if we could be sure that the fluid was clear and negative. I suppose that means negative for a Wassermann as well as other things. Therefore I suppose we can say that the cerebral symptoms were not due to lues. If it were due to metastatic malignant disease it would surprise me a little to have her improve rather than continue to get more confused. I should be inclined to think that the cerebral accident was due to hemorrhage or thrombosis rather than to malignant metastases, although she may have had malignant metastases to the brain. She probably did have malignant metastases to the lung.

I should be inclined to favor the diagnosis of primary adenocarcinoma of the fundus of the uterus with secondary involvement of the sigmoid or high rectum, and a generalized carcinomatosis otherwise, and burnt-out lues.

Clinical Discussion

Dr. Ernest M. Daland: I examined the patient an hour or two after she came into the hospital and at that time she said nothing about any rectal symptoms but spoke only of her vaginal bleeding. I did a pelvic and rectal examination on her at that time. She had this large mass slightly to the right. It was freely movable and smooth and it seemed like a large fibroid although the possibility of an ovarian cyst was considered. It did not feel like carcinoma of the fundus. It was too large and not firmly fixed. That afternoon when the history was more carefully taken the rectal bleeding was brought out. The next morning I did a proctoscopy. This was done without any difficulty in the knee-chest position. The proctoscope passed eight and a half inches. I could not inflate the bowel above that, and, as the history says, she showed a narrow slit with bleeding coming from the slit. The specimen was taken with a curet through the slit. I could not see any definite growth through the edge of the slit. It looked granular. We got a poor specimen which grossly we could not diagnose. The appearance was not that of carcinoma arising in the sigmoid.

Dr. Charles S. Kubik: I saw the patient a short time after the cerebral accident. Some improvement had already taken place and so I thought it was vascular occlusion, that is thrombosis or embolism, rather than hemorrhage, and because it was stated that at the onset the pupils were constricted and both plantar reflexes were extensor in type I was inclined to think that the trouble was in the basilar artery.

Clinical Diagnoses

Adenocarcinoma of the sigmoid.
Tertiary lues.
Cerebral thrombosis.
Bronchopneumonia.
Arteriosclerosis.

Dr. Arthur W. Allen's Diagnoses

Adenocarcinoma of the uterus.
Secondary involvement of the sigmoid.
Metastatic carcinoma, possibly of the lung and brain.
Cerebral thrombosis.
Tertiary lues.

Anatomic Diagnoses

Adenocarcinoma of the uterus with infiltration of the rectal wall.
Peritonitis, acute localized.
Atrophy of the right kidney.
Compensatory hypertrophy of the left kidney.
Hydronephrosis, left.
Hydroureter, left.
Pulmonary edema, slight.
Arteriosclerosis, marked, aortic.

Pathologic Discussion

Dr. Mallory: The biopsy which was taken, as Dr. Daland has described, showed a superficially normal mucosa underlying which in the submucosa islands of definite adenocarcinoma could be seen. One might be tempted to conclude from such findings that the gut was invaded from without but that would be very dangerous since often rectal biopsies are taken not from the center of the tumor but from the edge, and we frequently find normal mucosa overlying cancer which is infiltrating laterally. So that our suspicions were not aroused at all and knowing nothing of the story at that time we assumed that it was a primary carcinoma of the bowel.

The autopsy showed that it was not that but a primary uterine cancer which had grown upward and laterally to involve nearly sixteen centimeters of the upper rectum and sigmoid. The tumor mass seemed at first very hard and firm but as we cut into it we found there was simply a shell of tumor on the outside and the center was composed of gelatinous, necrotic material. The terminal ileum also had become involved in the tumor and two or three loops were firmly adherent to it. Between these loops we found a small abscess about eight centimeters in diameter filled with pus. It is not very clear that that played any part in the symptomatology. We found, as is so common in carcinoma of the uterus, practically no metastases. In other words, all the tumor present was direct extension from the uterus. The lungs, liver, brain were all free from metastases.

The brain lesion turned out to be localized infarct in the left globus pallidus.

One other rather striking feature at the autopsy table, but of no importance whatever in the clinical course of the disease, was a completely atrophic right kidney with an imperforate ureter on that side. On the other side we of course found compensatory hypertrophy, and there was also a moderate degree of hydronephrosis and dilatation of the upper part of the ureter with obstruction lower down where it passed beneath the tumor mass.

A PHYSICIAN: Were there any syphilitic lesions anywhere?

DR. MALLORY: No anatomical trace of them.

The heart was entirely negative except for very slight hypertrophy.

DR. JAMES H. MEANS: What was the exophthalmos?

DR. MALLORY: I am not clear about that, Dr. Means. It was not very evident on the autopsy table. It may have been a transitory affair. Have you any explanation, Dr. Kubik?

DR. KUBIK: No; I do not recall that as being a striking feature. She may have had simply a myopia.

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THE IMPORTANCE OF RECOGNIZING CHRONIC CONSTRICTIVE PERICARDITIS (PICK'S DISEASE)

It has become of far more than academic interest to recognize chronic constrictive pericarditis, for it has been proved recently that a considerable percentage of the cases, formerly incurable, can now be completely relieved by surgery consisting of pericardial resection. It is not a common disease but neither is it excessively rare for in three clinics alone in this country (one in Boston, one in Cleveland, and one in Nashville) in the last few years at least forty cases have been recognized at the last count (spring of 1935) and fourteen have been cured. Others throughout this country and in Germany have also been relieved by pericardial resection.

Three essentials for a successful operation have recently been outlined by White in the St. Cyre's Lecture of the National Hospital for Diseases of the Heart at the Royal Society of Medicine in London[1]. They are first, a correct diagnosis, secondly, selection of a patient who is seriously crippled by the disease and yet a satisfactory risk for operation, and thirdly, an experienced thoracic surgeon. In the series of fifteen cases presented by White, Dr. E. D. Churchill of the Massachusetts General Hospital effected cures in six and a large measure of improvement in one other out of ten cases on whom he operated.

The following definition and diagnostic clues have been offered by White. "Chronic constrictive pericarditis consists of a chronic fibrous or callous thickening of the wall of the pericardial sac which is so contracted that the normal diastolic filling of the heart is prevented." The points for diagnosis are (1) the insidious development of dropsy in a young or middle-aged person without previous disease of heart or kidneys, (2) preponderant liver enlargement and ascites, (3) the presence of little or no cardiac enlargement, (4) increased prominence of the neck veins—a very important sign, (5) small pulse pressure, often with "paradoxical" (Griesinger-Kussmaul) pulse, (6) x-ray evidence (poor pulsation of entire heart or of right heart border alone, calcification, chronic pleuritis), (7) abnormal electrocardiogram (low voltage or low or inverted "coronary" T waves in chronic disease in early youth), and (8) a previous history of acute pericarditis. The first, third, fourth, and seventh of these clues are the most important and consistent ones.

The three conditions with which chronic constrictive pericarditis has been usually confused are the ordinary portal cirrhosis of the liver, chronic heart disease (in particular, mitral stenosis) with congestive failure, and acute or subacute polyserositis (which is Concato's, not Pick's disease). From portal cirrhosis of the liver chronic constrictive pericarditis is to be distinguished chiefly by two signs (in the absence of complicating heart disease): (1) engorgement of the neck veins, and (2) abnormal electrocardiogram. From heart disease chronic constrictive pericarditis is to be distinguished by the absence of characteristic murmurs, especially the diastolic murmur of mitral stenosis, and of much cardiac enlargement. Actually heart disease itself is found with only the greatest rarity complicating chronic constrictive pericarditis. And finally, from acute or subacute polyserositis chronic constrictive pericarditis is to be distinguished by the absence of evidences of infection (fever and leukocytosis) and of friction rubs (of acute pleuritis or acute pericarditis), and by the presence of increased systemic venous pressure (except when there is a pericardial effusion as a part of the acute polyserositis). In this connection it is important also to call attention to a frequent error, namely that of considering perihepatitis or Zuckergussleber (frosted liver) and perisplenitis as a necessary part of the clinical entity of chronic constrictive pericarditis. There may or may not be a chronic peritonitis, involving capsule of liver

or spleen, as a part of a chronic polyserositis which may accompany Pick's disease; the pericardium may be the only serous sac involved in this disease and the liver capsule may be clear and glistening even though the liver is enlarged. The degree of hepatic cirrhosis in cases of chronic constrictive pericarditis as a rule is relatively slight. Conversely there are cases of chronic peritonitis with the liver not enlarged but closely encased in a thick capsule with no evidence of chronic constrictive pericarditis.

REFERENCE

1. White, P. D.: Chronic Constrictive Pericarditis (Pick's Disease); Treated by Pericardial Resection. Lancet 229: 539, 597 (Sept. 7, 14) 1935.

PROGRESS IN MEDICAL EDUCATION

The statistical review of medical education in the United States for the past year, recently published in the *Journal of the American Medical Association*[1] presents material which deserves consideration by every person interested in that fascinating subject, but especially by every physician. In the comment accompanying the review are suggested some trends, the importance of which one can only guess.

The problem of relieving suffering and of overcoming disease confronts the physician daily, in fact many times a day, and in an important sense schools of medicine are springs which supply the rivers of healing. Physicians must be interested in every fact pertinent to the question of how this primary problem concerning the springs is being solved, or at least is being attacked.

Excellent reviews of recent progress in the various branches of medicine have been issued in the literature, notable among them being the articles on medical progress in the past twenty-five years which appeared in the *British Medical Journal*[2].

The time is ripe for a study of the progress in medical education which has been made in the twentieth century. A superficial survey has been presented by the statistical studies, to one of which reference has already been made, but what is needed is a more penetrating analysis which will note the new ideas, their introduction, their spread, their influence, perhaps advancing, perhaps receding, their results, possibly their relatively permanent contribution to education.

There is, for example, the idea of a university. This was relatively slight in its influence in American medical education in 1900, yet of all ideas now working themselves out, it has wrought, perhaps, the greatest transformation. Most medical schools are associated with universities. To what extent are they dominated by the idea of university education? It is reported that educational methods appropriate for secondary school have been hyper-extended into the medical departments of some so-called universities. There is still much opportunity for improvement.

Another idea growing in importance of influence of late is that the patient, the concrete person who is sick, is the focus of interest for the medical student as well as for the physician and should be recognized as such. Then the old idea of learning by doing, applied especially in the internship, is receiving more widespread attention.

A fourth idea, vague, threatening, portentous, is the socialization of medicine. Few of us, if any, know just what this means. Its manifold connotations bewilder us. We are sure all is not well with the world of the practice of medicine. Some say it is the "individualization" of medicine that is the matter. Others say that medicine is essentially individualistic, and physicians are in their nature individualists. Then there is the retort discourteous that individualism is a cloak for selfishness.

It is too soon to record the influence of this fourth idea; it has hardly begun its course in its modern form and certainly it demands study. But those ideas mentioned first and others which might be noted have obviously been at work for years and of their effect too little has been said.

What we want to know is what progress has been made in this, the latest, of the centuries, in educating physicians. It is not merely what increase has there been in the information which every physician or any physician, must have as part of his armamentarium, but what progress in method has been achieved so that with a given expenditure of time and effort, and if one may say so, of brains, there comes to the individual student more power as a physician. Here is a challenge indeed to the medical educator.

REFERENCES

1. J. A. M. A. 105: 677 (Aug. 31) 1935.
2. Brit. M. J. 1: 909 (May 4) 1935.

SIGNING THE PLEDGE

Many readers of the *Journal* who hold teaching appointments at the various universities have doubtlessly within the last few weeks been asked to take an oath of allegiance to the Constitution of the United States. This oath, made mandatory by an Act of the Great and General Court of Massachusetts, was the subject of considerable controversy a few months ago. It is now required of teachers in private institutions, and of school children.

There is no reason why any good citizen of the Commonwealth should stickle over his rights and his principles and refuse to take this oath, objectionable as the coercive method may be to him. True, such coercion may be opposed to the spirit of the Constitution which it professes

to uphold, but the oath itself will do no harm, nor will it serve any useful purpose.

Surely there can be no advantage in denying to our political guides an opportunity of rendering lip service to the ideals of robust Americanism, and, by twisting the American eagle's tail a little harder, make it scream a little more loudly.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

RICHARDSON, HORACE K. M.D. Tufts College Medical School 1905. Formerly, Senior Physician, Sheppard and Enoch Pratt Hospital, Towson, Maryland. Now, Assistant Medical Director, The Austen Riggs Foundation, Stockbridge, Mass. Consulting Psychiatrist, The Fairview Hospital, Great Barrington, Mass., and Mental Hygiene Clinic, House of Mercy Hospital, Pittsfield, Mass. His subject is "Psychopathy and the General Practitioner." Page 787. Address: P. O. Box 235, Stockbridge, Mass.

WETHERBEE, WINTHROP, JR. A.B., M.D. Columbia University College of Physicians and Surgeons 1931. Formerly, House Officer and Resident Physician, Fifth Medical Service, Boston City Hospital, and Resident Physician, Medical Out-Patient Clinic, Boston City Hospital. Now, Assistant in Medicine, Boston University School of Medicine. Address: 482 Beacon Street, Boston, Mass. Associated with him is

FOLEY, JOHN A. A.B., M.D. Harvard University Medical School 1915. Assistant Visiting Physician, Boston City Hospital. Associate Professor of Medicine, Boston University School of Medicine. Address: 464 Commonwealth Avenue, Boston, Mass. And

RESNIK, JOSEPH. B.S., B.E., M.D. Tufts College Medical School 1918. Physician-in-Chief, Department of Physical-Therapeutics, Boston City Hospital. Head of Department of Physical-Therapy, Greater Boston Hospital for Chronic Diseases (Bikur-Cholim), Roxbury, Mass. Address: 184 Bay State Road, Boston, Mass. Their subject is "Diathermy in Lobar Pneumonia." Page 796.

ARCHER, BENJAMIN H. A.B., M.D. Columbia University College of Physicians and Surgeons 1920. Assistant Visiting Physician, Lincoln Hospital, New York City. Formerly, Instructor of Clinical Medicine, Cornell University Medical College; Chief of Arthritis Section, Cornell Clinic; Chief of Arthritis Service, Mount Sinai Hospital. His subject is "Specific and Non-specific Arthritis (With Special Reference to Trauma)." Page 799. Address: 1964 Grand Concourse, New York City.

HALSTED, JAMES A. A.B., M.D. Harvard University Medical School 1930. Assistant in Medicine, Massachusetts General Hospital. His subject is "Gonadotropic Hormone (Prolan) in Relation to Carcinoma of the Cervix." Page 803. Address: 264 Beacon Street, Boston, Mass.

DAMESHEK, WILLIAM. M.D. Harvard University Medical School 1923. Associate Physician, Beth Israel Hospital. Physician, Boston Dispensary. Instructor in Medicine, Harvard University Medical School. Assistant Professor in Medicine, Tufts College Medical School. His subject is "Progress in Hematology (Late 1933 and 1934)." Page 805. Address: 371 Commonwealth Avenue, Boston, Mass.

The Massachusetts Medical Society

SECTION OF OBSTETRICS AND GYNECOLOGY*

C. J. KICKHAM, M.D., *Chairman*, 524 Commonwealth Ave., Boston, Mass.
R. S. TITUS, M.D., *Secretary*, 472 Commonwealth Ave., Boston, Mass.

WHAT IS YOUR OPINION AS TO THE DANGER OF BARBITURATES IN OBSTETRICAL ANALGESIA?

During the past five years, the use of the barbiturates in obstetrical analgesia has increased tremendously. The drugs in popular usage are sodium amytal and sodium pentobarbital (nembutal); the latter has been rapidly replacing sodium amytal. The employment of these medications has become so universal that they have often been given indiscriminately.

One of the pronounced disadvantages of the barbiturates is the extreme restlessness of the patient. Sodium pentobarbital has a more depressing effect upon the higher brain centers with a decreasing amount of excitement. Consequently, any patient who has been given these medications must be watched by a trained attendant, and it is therefore most unwise to administer these drugs to a patient who is having the baby at home. In the hospital, a nurse should be at the patient's bedside throughout the entire labor and also during the postpartum period until the patient has fully awakened. Many a patient, after delivery, has gotten out of bed and wandered around the hospital corridors. It is good policy not to give cardiacs any of the barbiturates.

The barbiturates should not be administered after the patient has eaten. In the first place, it is possible that the medication will not take effect inasmuch as it may be slowly absorbed;

*A series of short selected articles by members of the Section will be published weekly.
Comments and questions by subscribers are solicited and will be discussed by members of the Section.

and, secondly, much more important, should the medication be absorbed, there is definite danger of the patient losing her swallowing reflex and inadvertently inspissating some vomitus or mucus in the trachea. This has not been an infrequent occurrence, and mortalities have been reported in the literature.

The barbiturates are prone to stimulate the flow of mucus, sodium amytal being a worse offender than sodium pentobarbital. If the patient, therefore, shows a tendency toward mucus production, one should cut down the dosage of the barbiturates and keep her in a much more wakeful condition. A great many of these patients take gas oxygen, as a terminal anesthetic, very badly. They are prone to gag and vomit. Drop ether is much more satisfactory. In patients with upper respiratory infections or those with tuberculosis, barbiturates should not be administered. It is ideal, of course, to keep a patient comfortable especially if she has a long labor. In such cases, one should be very careful to administer very small dosages of the barbiturates so that the patient can be awakened to take fluids. If she is narcotized too deeply, she is quite apt to become dehydrated and also to develop acidosis.

The bladder, during labor, has always needed careful watching. Should the bladder become distended, there is a great possibility that the muscle fibers will become paralyzed and that the patient will consequently have urinary retention and be unable to void. If she is kept deeply narcotized, frequent catheterizations during labor are imperative. Likewise, following delivery, if she is too sleepy to void, the bladder should be emptied by catheterization ten hours after delivery even without apparent distention. In this way, much of the incidence of postpartum urinary infection will be avoided.

In conclusion, the barbiturates should never be administered to a patient at home. During labor and until fully awakened after delivery, a nurse should be in constant attendance. These drugs are contraindicated in cardiacs, in upper respiratory infections, tuberculosis, and if the patient has had a full meal. Drop ether is the most satisfactory terminal anesthetic. The bladder has to be carefully watched both during labor and during the postpartum period. In long labors, the patient should be kept semiconscious so that she can take plenty of fluids, thereby avoiding dehydration and acidosis.

THIRD ANNUAL POSTGRADUATE MEDICAL EXTENSION COURSE

The following sessions have been arranged by the Committee for the week beginning October 27:

Barnstable

Sunday, October 27, at 4:00 P.M., at the Cape Cod Hospital, Hyannis. Subject: Arthritis: (a) Medical Care of Patient in the Home. (b) Orthopedic Treatment in Hospital and Aids in Home Treatment. Instructors: L. T. Swaim and R. T. Phillips. J. I. B. Vail, Chairman.

Bristol South (Fall River Section)

Monday, October 28, at 4:00 P.M., at the Stevens Clinic of the Union Hospital, Prospect Street, Fall River. Subject: Pediatrics: Abdominal Disease in Childhood; Medical and Surgical Aspects. Instructors: S. H. Clifford and H. W. Hudson, Jr. Eugene A. McCarthy, Sub-Chairman.

Essex North

Friday, November 1, at 4:00 P.M., at the Hotel Bartlett, 95 Main Street, Haverhill. Subject: Ophthalmology and Otolaryngology: (a) The Major Hazards in Diagnosis of Diseases of the Eye, Ear, Nose and Throat as Seen in General Practice. (b) Special Treatment in Acute Medical and Traumatic Diseases of Eye. Emergencies Arising in the Treatment of the Ear, Nose and Throat. Instructors: L. G. Richards and W. P. Beetham. Francis W. Anthony, Chairman.

Essex South

Tuesday, October 29, at 4:00 P.M., in the Nurses' Home of the Salem Hospital, Salem. Subject: Cancer of Stomach; Bowel and Genito-Urinary Tract. Modern Care of Inoperable and the Incurable; the Development of Improved Methods of Caring for These Cases with Less Pain and Discomfort with Minimum of Drug Therapy. Instructors: Horatio Rogers and R. C. Graves. Walter G. Phippen, Chairman.

Hampden

Thursday, October 31, at 4:00 P.M., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and at 8:00 P.M., at the Holyoke City Hospital, Holyoke. Subject: Kidney and Bladder Diseases, A (Surgical.): Hematuria: Its Significance in Surgical Diseases of Kidney and Bladder. Instructor: W. C. Quinby. George L. Schadt and George D. Henderson, Chairmen.

Hampshire

Wednesday, October 30, at 4:15 P.M., in the Nurses' Home of the Cooley Dickinson Hospital, Northampton. Subject: Cancer of Stomach; Bowel and Genito-Urinary Tract. Modern Care of Inoperable and the Incurable; the Development of Improved Methods of Caring for These Cases with Less Pain and Discomfort with Minimum of Drug Therapy. Instructors: David Cheever, W. C. Quinby and M. C. Sosman. Robert B. Brigham, Chairman.

Middlesex East

Wednesday, October 30, at 4:00 P.M., at the

Melrose Hospital, Melrose. Subject: Lung Diseases: (a) Significance of Symptoms and Signs in Chronic Lung Disease; Tuberculosis, Bronchiectasis, etc. (b) The Value of Surgery in Above Disease Problems. Instructors: Cleaveland Floyd and H. F. Newton. Joseph H. Fay, Chairman.

Middlesex South

Tuesday, October 29, at 4:15 P.M., at the Cambridge Hospital, Cambridge. Subject: Kidney and Bladder Diseases, A (Medical.): Acute Nephritis — Etiology, Diagnosis and Treatment. Nephrosis and Its Treatment. Instructor: L. B. Ellis. Edmund H. Robbins, Chairman.

Norfolk South

Monday, October 28, at 8:30 P.M., at the Quincy City Hospital, Quincy. Subject: Diseases of the Liver; Surgical Problems in Diagnosis of Acute Disease of Gall Bladder and Liver. Instructors: F. D. Adams and W. R. Morrison. David L. Belding, Chairman.

Plymouth

Tuesday, October 29, at 4:00 P.M., at the Brockton Hospital, Brockton. Subject: Neurological Aids in the Diagnosis and Treatment of Disease from the Medical Viewpoint. Problems of History and Examination with Special Reference to (a) Neurosyphilis, Multiple Sclerosis and Other Degenerative Conditions. (b) Diseases with Acute Onset, such as Meningitis and Cerebral Accidents. Instructor: T. J. Putnam. W. H. Pulsifer, Chairman.

Worcester North

Friday, November 1, at 4:30 P.M., at the Burbank Hospital, Fitchburg. Subject: Kidney and Bladder Diseases, B (Medical.): Chronic Nephritis. Cardiorenal Disease. The Use of Diuretics. Instructor: J. P. O'Hare. Edward A. Adams, Chairman.

MISCELLANY

ANTERIOR POLIOMYELITIS CASES FOR 1935

WEEKLY LIST, OCTOBER 14-19

City or Town	
Attleboro	1
Dighton	3
New Bedford	2
Somerset	1
Brockton	3
Framingham	1
Hanover	1
Milton	1
Natick	1
Quincy	1
Randolph	1
Stoughton	2
Boston	9
Cambridge	2
Concord	1
Medford	1
Revere	1
Waltham	2
Watertown	1
Wellesley	1
Lowell	2
Lynn	1
Salem	2
Leicester	1
Worcester	4
Springfield	1
	47

HARVARD MEDICAL SCHOOL APPOINTMENTS AND RESIGNATIONS

RESIGNATIONS EFFECTIVE SEPTEMBER 1, 1935

George W. D. Hamlett, Research Fellow in Anatomy.

Robert Amory, Member of Epilepsy Commission.

APPOINTMENTS

From September 1, 1935 to April 1, 1936:

Albert E. Rauh, Research Fellow in Anatomy.

From November 1, 1935 to July 1, 1936:

Paul B. Cassaday, Research Fellow in Medicine.

For one year from September 1, 1935:

Enrique Savino, Research Fellow in Epidemiology (School of Public Health).

Carl T. Nelson, Instructor in Bacteriology.

Maurice Fremont-Smith, Instructor in Medicine.

Benjamin Castleman, Instructor in Pathology.

Gilbert Horrax, Instructor in Neurology, Courses for Graduates.

Kurt H. Semsroth, Teaching Fellow in Bacteriology.

Alfred Kranes, Assistant in Medicine.

Lowrey F. Davenport, Assistant in Medicine.

Isadore E. Budnitz, Assistant in Medicine.

William M. MacKay, Assistant in Medicine.

Benedict F. Massell, Assistant in Medicine.

Edgerton McC. Howard, Assistant in Neurology.

Christian F. Midelfart, Assistant in Neurology.

Hugh P. Newbill, Assistant in Neurology.

Meier G. Karp, Assistant in Orthopedic Surgery.

Quentin M. Geiman, Assistant in Comparative Pathology in Medical School and School of Public Health.

Neils L. Anthonisen, Assistant in Psychiatry.

Grosvenor B. Pearson, Assistant in Psychiatry.

John D. Stewart, Assistant in Surgery.

Frederick W. Klemperer, Research Fellow in Biological Chemistry.

Georges J. P. Hornus, Research Fellow in Bacteriology.

James G. M. Hamilton, Research Fellow in Medicine.

Francis J. C. Herrald, Research Fellow in Medicine.

Michel Pijoan, Research Fellow in Medicine.

John A. V. Davies, Research Fellow in Pediatrics.

David Weinman, Research Fellow in Comparative Pathology.

Felix Deutsch, Research Fellow in Psychiatry.

Erik Homburger, Research Fellow in Psychology.

Georges E. P. Coppee, Research Fellow in Physiology.

DR. GASSER SUCCEEDS DR. FLEXNER

Dr. Herbert S. Gasser has been appointed to the position of Director of the Rockefeller Institute for Medical Research to fill the position made vacant by the resignation of Dr. Simon Flexner. Dr. Flexner has been given the title of Director Emeritus after thirty-two years of service.

Dr. Gasser was formerly Professor of Physiology and Director of Physiological Laboratories at the Cornell University Medical College.

A TESTIMONIAL DINNER AND MEETING IN HONOR OF DR. DAVID L. EDSALL

A testimonial dinner, in honor of Dr. David L. Edsall, recently retired dean of the Harvard Medical School, was held by the Harvard Medical School Alumni Association at the Harvard Club of Boston, Wednesday evening, October 23. President James B. Conant, of Harvard, presided, and Dr. A. Lawrence Lowell, president-emeritus of Harvard, delivered the principal address. Dean Charles S. Burwell, of the Harvard Medical School, also spoke.

Preceding the dinner, a meeting was held at the Harvard Medical School. Addresses on "The Development of Medical Education in the United States Since the World War" were made by Dr. Walter A. Jessup, President, Carnegie Foundation for the Advancement of Teaching; Dr. Eugene DuBois, Professor of Medicine, Cornell University; and Dr. Lawrence J. Henderson, Professor of Chemistry, Harvard University. Dr. Walter B. Cannon, Professor of Physiology, Harvard, presided. Members of the medical profession in the Boston area were present.

APPOINTMENT OF DR. HOSEA W. McADOO

The appointment has been announced of Dr. Hosea Webster McAdoo as medical director of the Ring Sanatorium and Hospital in Arlington, Mass. Dr. McAdoo, a Texan by birth, was graduated in medicine from Tulane University in 1920. After serving a year's internship at the Southwestern Railroad Hospital in St. Louis, he was resident physician for two years at the Warren State Hospital, Pennsylvania. This was followed by a three months' period as psychiatrist in St. Elizabeth's Hospital in Washington, D. C. From 1924 to 1929 he was medical officer in psychiatry in the United States Veterans Hospital at Little Rock, Arkansas, and from 1929 to 1930 assistant professor of pathology at Baylor University in Dallas. Dr. McAdoo became clinical director of the Springfield State Hospital in Sykesville, Maryland, in 1930 and was appointed superintendent in 1932, a post which he held up to the time of his present appointment.

CORRESPONDENCE

DIABETES AND CHRISTIAN SCIENCE

October 7, 1935.

Editor, *New England Journal of Medicine*,

Within the past few weeks I have had to attend two diabetic patients who had been treated with Christian Science and were in coma when I saw them. One of them I had seen in consultation ten years before. She followed medical advice for a time with satisfactory results, but later succumbed to the teachings of Christian Science. Diet and insulin were discarded. When I saw her again two months ago, she was greatly emaciated, stuporous and acidotic and vomited persistently. Her family very sensibly had called their former family physician at the beginning of this episode. She was immediately removed to the hospital and after a strenuous three-day battle was out of danger.

The other patient, seen first by me about a year ago, came at the insistence of a relative, a physician, but made only one visit and did not accept medical advice. A month ago the call came to see her again. She was in deep coma and had been so for more than twenty-four hours. Her attending Christian Science friends had refused to call medical aid. This patient, also, was removed to the hospital, but despite heroic treatment did not regain consciousness and died a few hours later.

The question arises: Is this manslaughter? It certainly is not science, and I doubt that it is Christian.

I believe that Christian Science is a helpful form of psychotherapy, but its practitioners should recognize its futility in organic disease.

Very truly yours,

HELMUTH ULRICH.

99 Bay State Road,
Boston, Mass.

RECENT DEATH

FALLON—JOSEPH FRANCIS FALLON, M.D., of 440 Boylston Street, Brookline, Massachusetts, died at his home, October 14, 1935. Dr. Fallon was born in Brookline in 1882 and after graduating from Boston College, entered Jefferson Medical College and was given his medical degree in 1908. He served his internship at the Bellevue-Governeur Allied Hospitals in New York and took a postgraduate course in London.

He served in the World War with the rank of lieutenant in connection with the transportation of troops.

Dr. Fallon joined the Massachusetts Medical Society in 1912 and was a member of the American Legion, the Clover Club and the Brookline Lodge of Elks.

He is survived by his widow, two sons, two daughters, two sisters and a brother.

OBITUARY

HENRY JOSEPH FITZSIMMONS, A.B., M.D., F.A.C.S.

FEBRUARY 21, 1880-OCTOBER 5, 1935

"A talented, honest, generous, serviceable man." Thus is the Honorable Patrick Andrew Collins, former mayor of Boston, characterized on the statue erected to his honor. This is saying much of a man and all of these epithets may with equal truth be applied to Henry Joseph FitzSimmons. Gentleness also was his in attitude and action. His passing removes a living example of conduct which has been helpful to younger medical men. It will continue to endear him to those of us who walked the same paths as he.

Born on February 21, 1880, he was graduated from Harvard College in 1903, and received his medical degree also from Harvard in 1908. His first internship of eighteen months was on the Surgical Service of the Boston City Hospital, after which he became Resident Surgeon at the East Boston Relief Station. After completing with distinction a six months' internship on the Orthopedic Service of the Boston Children's Hospital, he determined to make orthopedic surgery his chief concern, and was awarded a traveling fellowship for two years by the Boston Children's Hospital. These two years between 1910 and 1912 were profitable ones spent under masters of orthopedic surgery: Six months with Sir Robert Jones during part of which he was Resident Surgeon at the Liverpool Royal Southern Infirmary; work in the clinics of Calvé and Mennard at Berck Plage; work under Lamy in Paris, Putti in Bologna, Schanz in Dresden, Bielsalski in Berlin, Lange in Munich, and in the orthopedic clinics of Rome and Vienna. While in Munich, Lange perfected his original technique for the implantation of silk artificial ligaments and tendons. The young American orthopedic surgeon became one of his favorite pupils. FitzSimmons may be said to have introduced the method into this country. Upon his return from Europe, he familiarized himself with the type of work being done in the orthopedic clinics of Baltimore, Philadelphia, New York, Chicago and Rochester, Minnesota. He settled in Boston, was appointed a Junior Surgeon at the Boston Children's Hospital and had advanced to the position of full Visiting Surgeon and Instructor in Orthopedic Surgery at the Harvard Medical School at the time of his death.

He was consulting Orthopedic Surgeon to the Quincy City Hospital, the Choate Hospital in Woburn, the House of Providence in Holyoke, and St. Margaret's and St. Mary's Infant Asylum, and for many years conducted at regular intervals an Orthopedic Clinic at the Day Nursery in Holyoke, Massachusetts.

During the World War he enlisted in 1918 in the Medical Officers' Reserve Corps with the rank of Captain and saw service at Camps Greenleaf, Fort Oglethorpe, McPherson, Devens and finally at Base Hospital No. 10, Parker Hill, Roxbury, Massachusetts, being honorably discharged June 20, 1919.

Dr. FitzSimmons was married in 1914 to Elizabeth Rogers. His wife and four daughters survive him.

He was a member of the American Medical Association, American College of Surgeons, American Academy of Orthopedic Surgeons, Massachusetts Medical Society, Eastern States Orthopedic Club, Boston Orthopedic Club, Aesculapian Club, Military Order of the World War and the Charitable Irish Society.

Clinical work absorbed most of this busy surgeon's time, but he managed to carry out over a series of years important research studies as to the causes and treatment of Congenital Torticollis or "wry-neck." His conclusions were made authoritative by a large true end-result study. His final paper, published in The *New England Journal of Medicine*, July 13, 1933, is a noteworthy contribution.

One of Dr. FitzSimmons' close medical associates is unable to remember ever hearing him speak in derogatory terms of any of his professional associates and all of us were conscious of his infinite kindness. His medical opinion was honestly given and valuable. He was a most generous consultant whose mind was open. His devotion to his private, industrial and hospital patients was complete. His monument will be the abiding memory of a "talented, honest, generous, serviceable" gentleman.

R. B. O.

NOTICE

MEDICAL CLINIC AND STAFF ROUNDS AT THE PETER BENT BRIGHAM HOSPITAL

At 3:30 P.M. on Thursday, October 31, in the amphitheater of the Peter Bent Brigham Hospital, Dr. Henry A. Christian, Physician-in-Chief, Hersey Professor of the Theory and Practice of Physic in the Harvard Medical School, will give a medical clinic. To it are cordially invited practitioners and medical students. These clinics will be repeated on Thursdays, October to May.

On Saturdays in the wards of the Peter Bent Brigham Hospital, from 10 to 12, staff rounds will be conducted by Dr. Christian.

REPORT AND NOTICES OF MEETINGS

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

OCTOBER 9, 1935, HOTEL CONTINENTAL, CAMBRIDGE

Nearly two hundred and fifty Fellows were assembled to honor Dr. Charles E. Mongan, an outstanding member of this district society and recent-

ly elected President of the Massachusetts Medical Society.

The meeting was called to order by the district President, Dr. Sumner H. Remick, after a luncheon had been served.

The minutes of the previous meeting were accepted unread.

Dr. Alexander A. Levi, the secretary, next summarized the present status of the various hospitals in the district in relation to the following resolutions which were adopted at a meeting held during October, 1934:

Resolution (1) That the Trustees of Hospitals in this district be requested to make all industrial accident cases private patients in the hospital.

Resolution (2) That the Trustees of Hospitals in this district be requested to require from each patient applying for ward service a letter from a physician certifying that it is a suitable case for such service.

Up to the present the resolutions have been adopted and are functioning in the following-named hospitals:

(1) Charles Choate Memorial Hospital
(2) Framingham Union Hospital
(3) Newton Hospital
(4) Middlesex Hospital
(5) Symmes Arlington Hospital
(6) Whidden Memorial Hospital
(7) Waltham Hospital
(8) Winchester Hospital
(9) Somerville Hospital
(10) Malden Hospital
(11) Leonard Morse Hospital.

The resolutions have not as yet been adopted by:

(1) The Lawrence Memorial Hospital ("Some action taken by board.")

(2) The Marlborough Hospital ("No action taken by board of trustees.")

A second letter requesting information as to whether any action had been taken by the Board of Trustees of the Cambridge Hospital and the Emerson Hospital to date has remained unanswered. The first letter acquainting these institutions with the resolutions as adopted by the Middlesex South District Medical Society was sent during December, 1934 and a second was sent during September, 1935.

Dr. Edward J. O'Brien, Jr., a member of the subcommittee of the Public Relations Committee, presented the following report:

"(1) The committee composed of representatives from Norfolk, Middlesex South and Suffolk District Societies of the Massachusetts Medical Society to study and work on the abuse of medical charity in the City of Boston has been active during the summer months and now wishes to make a report of progress and some recommendations.

"The committee has studied conditions covering the admission of patients to the Peter Bent Brigham Hospital, Massachusetts General Hospital, Boston City Hospital, Children's Hospital and the Boston Dispensary.

"With the exception of the Boston City Hospital, there are theoretical safeguards against the abuse of charity. Since April, 1935, the Boston City Hospital has promised to place some social workers in the Out-Patient Department in order, theoretically at least, to control the abuse of charity which is admitted by its trustees to exist there. Up to October 5, 1935, when this report was written, the social workers had not begun to operate.

"In July, 1935, your committee asked the Boston Dispensary to admit to its Evening Pay Clinic only patients referred by physicians. The officers of the Boston Dispensary said that they would take this suggestion under consideration and report on their decision. No report has as yet been received.

"Your committee believes that theoretically the Department of Health of the City of Boston tries to stimulate the public to go to private physicians for well baby clinic work and preventing tuberculosis work. If, however, the patients do not employ private physicians for this work, the Health Department makes no provision at these clinics run by the Department to separate those who can afford to pay from those who cannot. The reason they do not make this attempt is because the Department considers the work educational and fears that if patients were refused admission, the educational aspects of this work would be interfered with. Only preventive work is done at these clinics. Practically the same condition exists in regard to immunization work.

"(2) Several specific instances of doctors referring patients for operation to the charity services in hospitals in the City of Boston were cited. It is hoped that the physicians of the District Societies will pay attention to the votes passed by the District Societies urging the doctors not to try to have charity work done on their patients who are able to pay.

"Your committee is interested in the experiment being tried in the District of Columbia on 'The Coördination of Resources for Medical Care in the District of Columbia' and wonders if some such program might not be worked out in Boston. It is felt that if this or some other program is to be worked out, the guiding force should be the recently established Hospital Council of Boston.

"In view of the above it is moved that each of the District Societies included in the City of Boston urge the Hospital Council to take active steps to eliminate the abuse of charity not only theoretically but practically in the free clinics for medical service in the City of Boston.

"It is further moved that each of the District Societies situated in the City of Boston urge its members to organize for immunization work at a fee commensurate with the ability of the patients to pay."

The report and the two motions contained in it were adopted by unanimous vote.

Dr. Edward J. O'Brien, Jr., then presented the following motion:

"Resolved: That the Secretary of the Middlesex South District be instructed to communicate either by letter or postal card with each member of the Middlesex South District, informing him of the abuses of medical charity and asking for aid and coöperation by not referring to charitable institutions or clinics persons who are able to pay for medical services." It was seconded and unanimously accepted without debate.

Dr. William R. Morrison, the Chairman of the Committee of Arrangements for the Annual Meeting of the Massachusetts Medical Society, was next introduced. He described some of the plans which had been made and urged the members to attend the annual meeting to be held in Springfield, June 8, 9, 10. As an added inducement he stated, the charge for the annual dinner would be one dollar only.

Dr. Reginald Fitz, associate professor of medicine at Harvard University Medical School, was then presented. He spoke of his fond regard for Dr. Mongan. He said, "Dr. Mongan as a member of the House of Delegates of the American Medical Association probably knows more doctors than any one other than Drs. Morris Fishbein and Olin West"; that "most of us make bad 'citizen-doctors' but Dr. Mongan has taught me what it means to be a good medical citizen."

Dr. Henry D. Chadwick, Commissioner of the State Department of Health, then addressed the members and acquainted them with some early history of the Massachusetts State Department of Health. He concluded his remarks by offering the felicitations of his Department to Dr. Mongan and the Massachusetts Medical Society and stated that he would coöperate in every way possible to improve the circumstances of the public and physicians in Massachusetts.

Dr. Charles E. Mongan who was next asked to speak was greeted by his fellow members. The continuous applause indicated the esteem and good feeling in which the Society holds him. After thanking Dr. Remick and the two preceding speakers, Dr. Mongan covered the wide field of economics and how it applies to medicine. He felt that he has "a mission to perform—namely, to sell the Medical Society to its members"; that "the Medical Society has every reason to be proud of its achievements and therefore expects the right to be heard in the Legislature as experts." Dr. Mongan stated, "The welfare of the people is the fundamental purpose of all these laws.

"The medical man is a cog in this thing called culture or civilization. You are loyal—you are willing. However, you need to be directed. You can do a great deal of work to prevent the lowering of the standard of living in Massachusetts; to improve the standards of medical education and to increase your sense of proprietorship in the Society." He asked the members to serve on committees when asked to do so and gave it them in charge to help carry out the traditions of the practitioner in Massachusetts.

The meeting was then adjourned.

ALEXANDER A. LEVI, M.D., *Secretary.*

HAMPDEN DISTRICT MEDICAL SOCIETY

The regular Fall Meeting of the Society will be held at the rooms of the Springfield Academy of Medicine, 20 Maple Street, Springfield, on Tuesday, October 29, 1935, at 4:15 P.M.

Paper for the afternoon: "Recent Advances in Medicine," Dr. Reginald Fitz of Boston. Discussion by Fellows.

Supper at 6 P.M. at expense of Society.

HERVEY L. SMITH, *Secretary.*

Censors meet for examination of candidates in the rooms of the Academy on Thursday, November 7, at 4 P.M.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

CENSORS' MEETING

Censors' Meeting at the Hotel Bartlett, Main Street, Haverhill, at 4 P.M., Thursday, November 7, 1935. Candidates must present applications and show diplomas to Secretary at least two weeks in advance.

E. S. BAGNALL, M.D., *Secretary.*

MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS

FALL MEETING AND DINNER

The Copley-Plaza, Wednesday, October 30, 6:30 P.M. $2.50 per plate.

Subject: Symposium on Silicosis and Asbestosis.

This will be an extremely interesting meeting, and a large attendance is desired.

GEORGE H. R. GOSMAN, M.D., *President,*
WM. P. COUES, M.D., *Secretary.*

NORFOLK DISTRICT MEDICAL SOCIETY

A stated meeting of the society will be held in the Sharon Sanatorium, Sharon, Mass., on Tuesday, October 29. Telephone Sharon 2172.

PROGRAM

4:00 to 4:30 P.M.—Ward Visits.
4:30 to 5:00 P.M.—Business Meeting.
5:00 to 6:00 P.M.—Communications.

The Early Diagnosis of Tuberculosis. Dr. Walter A. Griffin.

The Treatment of Bronchiectasis. Dr. Edward D. Churchill.

A collation will be provided following the presentation of the papers.

From Dedham rotary traffic circle proceed on Providence route 1 for eight miles turning left on route 27 and continuing thereon for 2 2/3 miles to sanatorium entrance.

From Mattapan Square proceed through Canton to Sharon Square and thence to sanatorium.

FRANK S. CRUICKSHANK, M.D., *Secretary.*
1236 Beacon Street,
Brookline, Mass.

SUFFOLK DISTRICT MEDICAL SOCIETY

CENSORS' MEETING

The Censors of the Suffolk District Medical Society will meet for the examination of candidates at the Medical Library, 8 Fenway, Thursday, November 7, 1935, at 4:00 o'clock.

Candidates should make personal application to the Secretary, and present their medical diplomas at least one week before the examination.

CHARLES C. LUND, *Secretary.*
319 Longwood Avenue, Boston.

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, OCTOBER 28, 1935

Monday, October 28—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. G. I. Clinic. Case Presentation. Dr. K. S. Andrews.

*8:15 P.M. New England Heart Association. Massachusetts General Hospital, Ether Dome.

Tuesday, October 29—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. "Flat Feet." Dr. John D. Adams.

6:30 P.M. Massachusetts Psychiatric Society. Parker House, Boston.

Wednesday, October 30—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Ward Cases. Dr. S. J. Thannhauser.

†12 M. Clinico-Pathological Conference. Children's Hospital.

6:30 P.M. Massachusetts Society of Examining Physicians. Copley Plaza, Boston.

Thursday, October 31—

*8:30-9:30 A.M. Clinic, Surgical and Orthopedic Staffs of Children's Hospital, at the Children's Hospital.

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. "Revision of Interpretation of Laboratory Tests for Syphilis." Dr. Hinton.

*3:30 P.M. Medical Clinic at the Peter Bent Brigham Hospital.

Saturday, November 2—

*10-12. Staff rounds at the Peter Bent Brigham Hospital.

*Open to the medical profession.
†Open to Fellows of the Massachusetts Medical Society.

October 24—New England Society of Psychiatry will be held at the Medfield State Hospital, Medfield, at 12:30 P.M.

October 25—Boston University School of Medicine Surgical Clinic at the Boston City Hospital, Cheever Amphitheatre, 12-1.

October 28—William Harvey Society will meet at 8 P.M. in the Auditorium of the Beth Israel Hospital, Boston.

October 28—New England Heart Association will meet in the Ether Dome of the Massachusetts General Hospital at 8:15 P.M.

October 28 - November 1—The Twenty-Fifth Clinical Congress of the American College of Surgeons. See page 1065, issue of May 30.

October 29—Massachusetts Psychiatric Society will meet at 6:30 P.M. at the Parker House, Boston.

October 30—Massachusetts Society of Examining Physicians. See page 839.

October 31—Medical Clinic at the Peter Bent Brigham Hospital. See page 837.

December 5-7—National Society for the Prevention of Blindness. See page 795.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH DISTRICT MEDICAL SOCIETY

November 7—Censors' Meeting. See page 839.

HAMPDEN DISTRICT MEDICAL SOCIETY

October 29—See page 839.
November 7—Censors' Meeting. See page 839.

NORFOLK DISTRICT MEDICAL SOCIETY

October 29—See notice on page 839.

SUFFOLK DISTRICT MEDICAL SOCIETY

October 30—Stated Meeting. Boston Medical Library. "The Interpretation of Problems in Bright's Disease and Related Conditions," Dr. Soma Weiss. "The Management of the Problems in Bright's Disease and Related Conditions," Dr. Laurence B. Ellis. Discussion: Dr. George Gilbert Smith and Dr. Louis E. Phaneuf.

November 7—Censors' Meeting. See notice elsewhere on this page.

December 11—Joint Meeting with the New England Heart Association at the Boston Medical Library. "Constrictive Disease of the Pericardium," Dr. Charles Sidney Burwell. Discussion: Dr. Edwin D. Churchill and Dr. Paul D. White.

January 29, 1936—Joint Meeting with the Boston Medical Library at 8 Fenway. "Observations Around the World," Dr. Walter B. Cannon.

March 18, 1936—Meeting at the Boston Medical Library. "The Laboratory and Clinical Story of Fatigue," Dr. Arlie V. Bock and Dr. David B. Dill. Discussion: Dr. Donald J. McPherson and Dr. Augustus Thorndike, Jr.

April 29, 1936—Annual Meeting at the Boston Medical Library. "The Treatment of Septicaemia," Dr. Champ Lyons. "The Pleurality of Scarlatinal Streptococcus Toxin," Dr. Sanford B. Hooker. Discussion: Dr. Hans Zinsser.

The medical profession is cordially invited to attend all of these meetings.

ROBERT L. DeNORMANDIE, M.D., President,
CHARLES C. LUND, M.D., Secretary,
FRANCIS T. HUNTER, M.D.,
Boston Medical Library.

WORCESTER DISTRICT MEDICAL SOCIETY

November 7—Censors' Meeting will be held in the Library Rooms of the Worcester District Medical Library, Inc., 34 Elm Street, Worcester, at 4:30 P.M.

November 13—Wednesday evening. Grafton State Hospital, North Grafton, Mass. Dinner and scientific program. Subjects of program to be announced later.

December 11—Wednesday evening. St. Vincent Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

January 8, 1936—Wednesday evening. Worcester City Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

February 12, 1936—Wednesday evening. Worcester State Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

March 11, 1936—Wednesday evening. Memorial Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

April 8, 1936—Wednesday evening. Hahnemann Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

May 12, 1936—Wednesday afternoon and evening. Annual Meeting of Society. Time, place and details of program to be announced in an April issue of the Journal.

ERWIN C. MILLER, M.D., Secretary.

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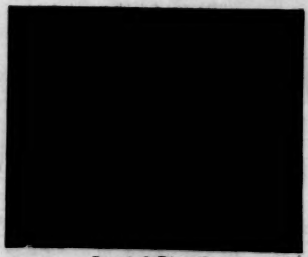

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1923

"Carbohydrates were added gradually. Dextri-maltose is apparently the best of the sugars."—*A. Bogen and G. Boyd: Acute intestinal intoxication in infants, Canad. Med. A. J. 13:900-908, Nov. 1923.*

1923

"With the protein milk feeding in a couple of days the stools become putty like and constipated. When this occurs we can gradually add dextri-maltose to the diet, finally working the baby back to a milk diet."—*F. B. Morgan: Underfeeding and fat indigestion in infants, Iowa Homeopathic J. 13:75-87, Aug. 1923.*

1924

". . . the ferment maltase which converts maltose into a monosaccharide evidently occurs in other parts of the body as well as the intestines because when it is injected subcutaneously it can not be recovered in the urine. This partly accounted for the fact that the power of assimilation of the body for maltose is twice that of the other two, as Czerny and Keller found. For this reason the possibility of over stepping the infant's tolerance for sugar is fifty per cent less when this sugar is used. In being more rapidly inverted and absorbed it is less liable to cause fermentation. Clinically these observations have been carried out and the consensus of opinion favors maltose as the sugar of choice. Czerny, Keller, Finkelstein, Langstein, and Meyer used it in a preparation consisting of about equal parts of dextrin and maltose with some sodium chloride."—*Artificial feeding of infants, International Med. Digest, 8:961-977, July 1924.*

1924

"In a communication published in 1918, the author reported striking results in eleven out of twelve cases, The initial mixture in most instances consisted of 270 c.c. skimmed milk, 360 c.c. water, 60 g. farina and 30 g. dextri-maltose boiled an hour or longer in a double boiler until sufficiently thick to adhere to an inverted spoon. . . . In 1921 his series of cases so treated had reached twenty-eight, with a mortality of 3.5 per cent."—*L. W. Sauer: Hypertrophic pyloric stenosis, Arch. Pediat. 41:145-170, March 1924.*

1924

In dyspepsia, "The carbohydrate must not be allowed to exceed 3 per cent. Dextri-maltose is the most suitable sugar."

In the treatment of decomposition (atrophy, malnutrition, marasmus), ". . . when there has been obvious improvement, dextri-maltose is gradually increased from 3 to 5 per cent."—*B. Myer: The nutritional disturbances of infancy, Brit. M. J. 1:1079-1083, June 21, 1924.*

1924

In acute dyspepsia, "Some carbohydrate is essential to promote water-retention in the tissues and prevent loss of weight, but only such carbohydrates should be selected as will produce the least intestinal fermentation, such as dextri-maltose, which may be administered at first in small quantities, increasing the amount every second day."

Concerning the treatment of diarrhea, "If the weight remains stationary, it is an indication that loss of substance is occuring through the stools, mostly in the form of alkaline salts. To equalise this loss of substance, the diet must be increased, but in such a way as to avoid causing fermentation. This may be done by adding dextri-maltose and preparations of protein to the food, increasing the calories until 'the infant is taking 160 calories per kilo. of body weight."—*H. L. Ratnoff: Nutritional disturbances, Arch. Pediat. 41:771, Nov. 1924.*

1924

"The most desirable sugar is dextri-maltose, because of all the sugars maltose is least apt to ferment."—*A. I. Bloe: The use of protein milk in pediatrics, Med. J. & Rec. 119:950, April 2, 1924.*

1924

"Maltose is absorbed in larger proportion than other sugars, breaks up into two molecules of dextrose, and often quickly gives a striking gain in weight."—*F. M. Fry: Fixed principles in the feeding of infants, Canad. M. A. J. 14:503-508, June 1924.*

1924

"The treatment of artificially fed children in the first of these groups consists in putting them on a low fat dietary, and giving them carbohydrate in the form of one of the less fermentable sugars—e. g., dextrimaltose."—*L. G. Parsons: Wasting disorders of early infancy, Lancet, 1:867-894, April 5, 1924.*

1925

"According to Finkelstein, infants will tolerate a much higher mixture of maltose and dextrin than either lactose or cane sugar."

"Milk sugar causes abnormal acid fermentation. This results in symptoms of intestinal irritation due to destruction of epithelium which interferes with the proper emulsification of fats; therefore, the presence of fats acts as an additional irritant and provokes loose bowels.

"When intestinal irritation exists, caused by the presence of milk sugar, the symptoms will continue even though the milk sugar has been greatly reduced, because even small quantities of this milk sugar will keep up lactic acid fermentation and consequent destruction of the epithelium."

"Cane sugar is less irritating to the intestinal mucosa than milk sugar. It is easily assimilated, and for this reason has many advocates. I have seen good results therefrom. When malt sugar cannot be procured, my advice is to use cane sugar."—*L. Fischer: Diseases of Infancy and Childhood, F. A. Davis Co., Phila., 1925, vol. 1, pp. 65, 66, 67.*

1925

"If, however, dyspepsia develops, the skimmed milk or calcium caseinate solution should promptly be given before each breast-feeding. Dextri-maltose should be added because of the great need of these small infants for a high caloric diet. This sugar does not readily ferment and is well tolerated."—*A. M. Donnenberg: Dyspepsia in the breast-fed, new-born infant: causes, symptoms and management, Arch. Pediat. 42:281-291, May 1925.*

1925

"In the treatment of diarrhea, "Dextri-maltose preparations are preferred, for they do not ferment readily, are rapidly absorbed and leave very little for fermentation."—*V. A. Hendon: Protein milks in infant feeding, Arch. Pediat. 42:745-760, Nov. 1925.*

1925

"Infants gain in weight when malt-sugar or the malt preparations are given."—*L. Fischer: The Health-Care of the Baby, Funk & Wagnalls Co., New York, 1925, p. 96.*

1925

"While it would seem on theoretical grounds that milk sugar should be chosen, we find in practice that dextri-maltose seems to be the kind of sugar that works best."—*F. H. Richardson: Simplifying Motherhood, G. P. Putnam's Sons, New York, 1925, p 140.*

1926

"There is no proof that milk sugar is necessary for the infant's nutrition, although it is this sugar that occurs in the milk of all mammals and there is abundant clinical experience to show that the other carbohydrates are just as beneficial and more easily digested."

"Malt sugar (maltose and dextrin), however, seems to be more easily digested and better taken care of by infants having had much digestive trouble."—*R. H. Dvenant: Simplified Infant Feeding, J. B. Lippincott Co., Phila., 1926, pp. 48, 61.*

1926

In intestinal intoxication, "I have had more experience with dried skimmed milk in which 2 to 5 per cent dextrimaltose, barley or rice flour has been cooked, and the mixture subsequently fermented by lactic acid bacilli or soured with lactic acid, than with any other food except protein milk."—*G. F. Powers: A comprehensive plan of treatment for the so-called intestinal intoxication of infants, Am. J. Dis. Child. 33-833-857, Aug. 1926.*

1926

"Preferably a dextrimaltose carbohydrate should be added after the bowel movements become thick and pasty."—*F. H. Harrell and E. Boyd: Dyspepsia in the breast-fed infant, Indiana M. J. 19:402-404, Oct. 1926.*

1926

In gastrointestinal disorders, "Dextri-maltose has been preferred to the other sugars as apparently less irritating."—*E. Carrie and U. Cox: The examination of the gastric contents in infants, with some considerations as to the value of lactic acid milk in infant feeding, Lancet, 2:388-395, Aug. 14, 1926.*

Continued down to 1936

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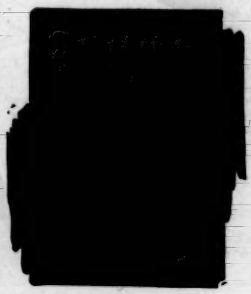

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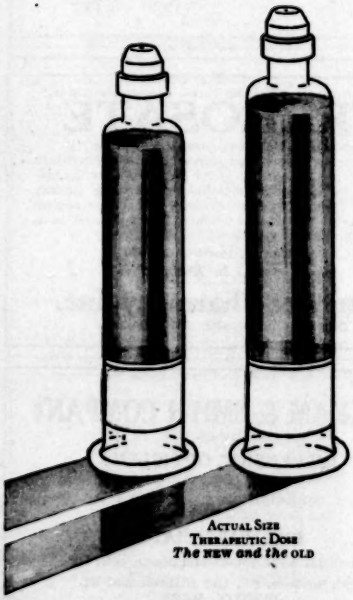

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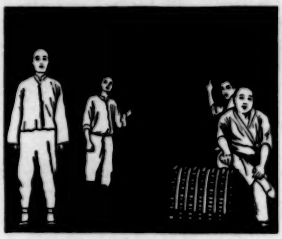

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